SCIENCE

VOL. 103 *Friday, April 12, 1946* NO. 2676

In This Issue

Published by the

American Association for the Advancement of Science

SCIENCE

Editor: Willard L. Valentine

Assistant Editor: Mildred Atwood *Advertising Manager:* Theo. J. Christensen

Policy Committee: Malcolm H. Soule, Roger Adams, Walter R. Miles and Kirtley F. Mather

VOL. 103 FRIDAY, APRIL 12, 1946 No. 2676

Contents

SCIENCE: A Weekly Journal, since 1900 the official organ of the American Association for the Advancement of Science. Published by the American Association for the Advancement of Science every Friday at Lancaster, Pennsylvania.

Communications relative to articles offered for publication should be addressed to Editor, Massachusetts and Nebraska Avenues, Washington 16, D. C.

Communications relative to advertising should be addressed to THEO. J. CHRISTENSEN, Massachusetts and Nebraska Avenues, Washington 16, D. C.

Communications relative to membership in the Association and to all matters of business of the Association should be addressed to the Permanent Secretary, A.A.A.S., Smithsonian Institution Building, Washington 25, D. C.

Annual subscription, $6.00 Single copies, 15 cents

Entered as second-class matter July 18, 1923 at the Post Office at Lancaster, Pa., under the Act of March 3, 1879.

SCIENCE

Vol. 103, No. 2676 Friday, April 12, 1946

Advisory Committee on Scientific Personnel

M. H. Trytten, *Chairman*

THE EXTENT OF SCIENTIFIC RESEARCH under government administration is clearly to be greater in the postwar years than ever in history. The military departments alone will be faced with the need for large-scale activities if they are to keep pace with the unfolding of science. But also the other departments having scientific responsibilities will need to enhance the pace and scope of their activities. These facts have led government scientists to see the need to improve the employment status of Civil Service scientists by revised Civil Service rules and regulations affecting scientific employees, so that government service in this field may achieve a career potentiality on a par with any other type of scientific employment.

To attain this end, there has been established by the Civil Service Commission an Advisory Committee on Scientific Personnel. The recommendation for the establishment of the Committee was made by the Council of Personnel Administration, the official government policy-forming organization in personnel matters. The members of the new Advisory Committee were named in each case by the Secretary of the Federal department represented. The chairman was selected from a nongovernment agency to provide representation of the point of view of organized science.

The activities of the ACSP have been in two main areas. Important from the first was the need to facilitate in-service training for the rather large army (ca. 5,000–10,000) of Federal scientific and technical employees at the graduate level in the Washington area. This problem has involved canvasses to determine course needs and course offerings, and efforts to assist in solving educational problems associated with this work. These and attendant problems are being met by an auxiliary committee, the Science Training Group, under the chairmanship of Dr. M. W. White, Dr. Philip Powers, secretary.

The other major area of interest of the ACSP has been in the regulations under which the scientific Civil Service works. Here, too, an auxiliary committee has been set up and has been working to develop concrete recommendations which, after concurrence by the senior committee, are then taken up by the ACSP with the Civil Service Commission and others for discussion. The members of the auxiliary committee on Civil Service regulations are: Dr. A. H. Hausrath, Navy Department; Dr. K. E. Lohman, U. S. Geological Survey; Dr. W. H. Larrimer, Department of Agriculture; Dr. M. J. Shear, National Cancer Institute; Dr. F. G. Brickwedde, National Bureau of Standards; Dr. R. C. Duncan, Naval Ordnance Laboratory; and Lt. Col. T. H. Whitehead, Chemical Warfare Service.

Perhaps from time to time some discussion of particular recommendations may occur in the scientific periodicals. In view of the increasing role of scientists in the Government, there can be no doubt that all scientists have a stake in the matter. Some recommendations have already been made, and, in fact, the Executive Order of 16 February 1946, providing for return of Civil Service to a peacetime status, includes several provisions reflecting the thinking of the Committee. Other recommendations are now under consideration. The article which follows is deemed of interest to scientists generally as a by-product of the considerations of this Committee.

Need for a Meaningful B.S. Degree

Advisory Committee on Scientific Personnel

Scientific groups have been much disturbed by the official interpretation of the Starnes-Scrugham Act of 1944, the so-called "Veterans Preference Act." This Act provides that:

> No minimum educational requirements will be prescribed in any civil-service examination except for such scientific, technical, or professional positions the duties of which the Civil Service Commission decides cannot be performed by a person who does not have such education. The Commission shall make a part of its public records its reasons for such decisions.

Before the passage of this Act the Civil Service Commission had automatically prescribed a four-year college education or its equivalent as the basic educational requirement for examinations for probational appointment in the P-1 and P-2 grades in the professional and scientific services of the Government. The restrictions in this Act on the use of minimum educational requirements, therefore, appeared a clear-cut case of the reduction of standards in the Federal scientific Civil Service. Recently the sentiment among scientists against such apparent lowering of standards became so strong that the National Academy of Sciences and the National Research Council became interested in the problem, and letters signed by Dr. Frank B. Jewett for the Academy and Dr. Ross G. Harrison for the Council were written to many scientific societies. They suggested that the scientific societies consider the matter and express their opinions in formal communications to the government officials dealing with the subject. As a result, a great number of letters have come to the National Academy of Sciences and the National Research Council, expressing the deepest concern over this problem.

The Advisory Committee on Scientific Personnel has given much time to the consideration of the Veterans Preference Act as it bears upon the matter of educational requirements for Federal positions. It has discussed the matter with the CSC and with veterans' organizations. In all these discussions it has been recognized by everyone that it is to the best interest of neither the government service nor the veteran to place any but the most highly qualified persons in the scientific staff of the Federal Government. The only point at issue, therefore, has been the long-time effect of the given clause on the quality of the scientific Civil Service.

Perhaps the most important single point raised in the Congressional discussions preceding the passage of the Starnes-Scrugham Act was the reliability of the Bachelor of Science degree as a measure of academic accomplishment. It was pointed out frequently that the standard for the B.S. degree in American colleges and universities is a highly variable quantity. In some cases a stiff professional curriculum is required, while in others, work in the major subject is extremely limited and much of that work may, in fact, consist of courses in the teaching of the subject and may therefore yield little in professional training of the type required for scientific work in the Government. There is also considerable variability as to nature and number of collateral courses prescribed. If the B.S. degree is to be demanded as a requirement and strictly adhered to, it might result in such absurd cases, for example, as that where a near graduate of a highly technical institution with a large percentage of required courses in the field would be turned aside, while the holder of a degree from an institution which required only the weakest major could be accepted. The point made by the veterans' organizations and many in Congress was that a criterion such as the B.S. degree could be demanded with consistency only when it was, in itself, a consistent measure of accomplishment or when it at least could be depended upon as the best available guarantee of a minimum level of preparation.

The ACSP believes the situation to be highly unfortunate, because it seems quite clear that a first line of defense against dilution has been lost by the removal from Civil Service entrance provisions of the requirement of a B.S. degree. It is possible to retreat to a second line of defense, which would mean the setting up of particular credit requirements such as, for example, 30 credit hours in the major subject and strongly contributing minor subjects. The obvious disadvantages of such a requirement need hardly be emphasized. It may be pointed out, however, that if only the credit requirements in chemistry, for example, be stated (e.g. 30 credits) and, as is required by law, posted in public places throughout the land, this may well act as an incentive to candidates to confine their training to the base minimum of such courses without collateral courses. And if additional collateral courses in neighboring fields be specified, it may in the long run serve to set up the CSC as a curriculum influence of importance in American college practice. It would be better if curricula were established by departments in the interest of a sound training rather than in the interest of meeting some particular formula laid down by the CSC.

This problem might not be deemed so important if employment by the Federal Government were a minor factor in the whole scientific employment pattern. It is already a major factor in certain fields, and its importance may extend to other fields as time goes on. Furthermore, the problem of meaningful B.S. degrees extends far beyond the Civil Service. The weakness of this degree as a criterion has frequently been embarrassing throughout the war period. It was a big factor in the Selective Service situation. Had professional B.S. curricula existed, it is possible that the Selective Service System would have been able to use them as criteria of minimum preparation for use in screening out those who should be given special consideration as scientists, thus obviating some of the cases of flagrant misassignments of scientific personnel. In assigning Federal fellowships or Federal monies for students in the early part of the war, the lack of such a recognized curriculum, or at least of some recognized standard of minimum preparation in the fields of interest, was felt.

Discussions on the proper type of organization for the mobilization of scientific personnel in wartime have been numerous during the war and since V-J Day, many of these have taken place among military personnel. Perhaps some type of organization similar to the Medical Corps will arise in time. If so, scientists will need to be commissioned from civil life on the basis of accomplishment. Again, a meaningful B.S. degree is necessary.

The present National Research Foundation Bill, sponsored by Senators Magnuson, Kilgore, *et al.*, (S. 1850), calls for the establishment of fellowships for advanced study. The same problem of threshold preparation for applicants will arise, and the existence of a meaningful B.S. degree would again be useful. The dominant role of American scientific education in the world today will mean that foreign students will come here more and more and that our students will go abroad. The American degree will then become to a greater and greater extent world currency in this field. It would be better in this connection, too, if a more uniform measure of accomplishment were represented by our B.S. degree.

These are indications that the Federal Government is being called on more and more frequently to deal with persons on the basis of their academic accomplishments. The law and regulations based on the law require the existence of definable terms. The B.S. degree at the present time is frankly not a sharply definable term. The ACSP is not presuming to suggest any particular action, but does feel a responsibility to present to the scientific population a situation which seems worth describing and which does seem to merit most thoughtful consideration.

Canadian Researches on BAL (British Anti-Lewisite)

Leslie Young

Department of Biochemistry, University of Toronto

ONE OF THE OUTSTANDING ACHIEVEMENTS in the field of chemical warfare research in World War II was the discovery by Peters, Stocken, and Thompson of the antidotal action of 2,3-dimercapto-propanol (BAL, British anti-lewisite) to lewisite and other arsenical compounds. Two reviews of work on BAL have been published recently. The first of these was by Peters, Stocken, and Thompson (*3*), and the second, which dealt particularly with researches on BAL in the United States, was by Waters and Stock (*11*). The purpose of the present article is to review briefly some researches on BAL conducted on behalf of the Directorate of Chemical Warfare, Department of National Defence, Ottawa.

Work on BAL was started in Canada late in 1941. The first investigation undertaken was a comparison of the antidotal activity and toxicity of BAL with those of a series of related compounds. In the course of this work the following thiols were synthesized (*4, 12*): 1,2-dimercapto-ethane, 1,2-dimercapto-propane, 1,3-dimercapto-propane, 1,2,3-trimercapto-propane, 1,2-dimercapto-n-butane, 1,3-dimercapto-2-propanol, 2,2′-dimercapto-diethyl ether, 3,3′-dimercapto-dipropyl ether, and 2,2′-dimercapto-diisopropyl ether. These compounds, together with 1- and 2-mercapto-propane and 2-mercapto-ethanol, were tested for antidotal activity to lewisite and toxicity when applied to the skin of the rat (*6, 12*). None of the compounds tested was found to be superior to BAL as an antidote to lewisite. Although none of the monothiols tested showed antidotal activity under the above conditions, all the dithiols and the trithiol studied gave evidence of some antidotal activity. Only in the case of 1,3-dimercapto-2-propanol did this activity approach that of BAL, however, and this compound proved to be much more toxic than BAL.

Rats usually die within 24 hours after the application of lethal amounts of lewisite ($2 \times LD_{50}$) to the skin. Almost invariably, however, the lives of the

animals are saved if BAL is applied to the dosed area of skin not later than two hours after dosing with lewisite. Even when treatment with BAL is delayed for a longer period, the animals sometimes survive (*6*). Protection against the systemic effects of lewisite in rats also occurs when BAL is applied to a skin site other than that contaminated with lewisite (*15*), or when BAL in propylene glycol solution is administered by intramuscular injection (*13*). Protective action is also obtained when BAL is applied to the skin two hours, or sometimes even longer, before application of lewisite to another area of skin (*15*)—a finding which can be explained by the low rate of percutaneous absorption of BAL in the rat (*10, 15*).

When applied to the skin of the rat, BAL exerts an antidotal action to sodium arsenite ($2 \times LD_{50}$) administered by intraperitoneal injection (*2*). When rats are dosed intraperitoneally with lethal amounts of cadmium chloride, they sometimes survive if treated percutaneously with BAL. There is evidence, however, that under some conditions deleterious effects follow the administration of BAL to rats poisoned with cadmium (*1*).

The finding of the Oxford workers (*3*) that there is an increased urinary excretion of arsenic following the administration of BAL to rats dosed with lewisite was confirmed and extended. Whether BAL is applied to the skin site contaminated with lewisite, or to a separate site (*14*), or given by intramuscular injection (*13*), the arsenic content of the urine excreted during the 24 hours after dosing with lewisite ($0.5 \times LD_{50}$) is markedly increased when the BAL is given immediately, one or six hours after the lewisite. When the administration of the BAL is delayed for 24 or 48 hours the effect on the urinary excretion of arsenic in the succeeding 24 hours is much less marked. The fecal excretion of arsenic is not influenced to a significant extent by BAL treatment.

Although BAL exerts an antidotal action in sodium arsenite poisoning, its influence on arsenic excretion under these conditions is slight (*2*). On the other hand, whereas rats given intraperitoneal injections of cadmium chloride ($0.5 \times LD_{50}$) show almost no urinary excretion of cadmium, they excrete considerable amounts of cadmium in the urine when also treated with BAL. This tends to prevent the accumulation of cadmium in the liver which occurs when BAL is not administered (*1*).

Radioactive BAL, *i.e.* 2,3-dimercapto-propanol with radioactive sulfur (S^{35}) incorporated in the molecule, was synthesized (*7*) and used in studies of the absorption and metabolism of BAL (*5, 8, 9*). The radioactive compound was obtained by allowing 2,3-dibromo-propanol to react in methanol with sodium hydrosulfide which had been prepared from hydrogen sulfide containing H_2S^{35}.

BAL penetrates skin rather slowly. In experiments with radioactive BAL the average rate of percutaneous absorption of BAL in the rat over a period of six hours was found to be 0.38 mg./cm.^{2} skin/hour (*8*). This value is of the same order as that obtained in preliminary experiments on the rate of absorption of BAL from human skin (*5*). When radioactive BAL dissolved in propylene glycol is injected intramuscularly into rats, it passes rapidly from the site of dosing, for almost no S^{35} is present in the dosed muscle six hours after injection (*9*).

In experiments in which radioactive BAL is administered to rats percutaneously (*8*) or intramuscularly (*9*), S^{35} is distributed throughout the organism and, apart from somewhat higher concentrations in the intestine and its contents and in the kidney, it does not appear to accumulate preferentially in any of the main organs. The most striking feature of such experiments is the rapidity with which S^{35} is excreted in the urine. For example, after an intramuscular injection of a solution of 20 mg. of radioactive BAL in propylene glycol, the amounts of S^{35} present in the urine at 6, 12, and 24 hours after injection corresponded to 45.5, 71.0, and 81.3 per cent, respectively, of the radioactive BAL administered (*9*). A similar rate of excretion of S^{35} is observed when radioactive BAL is administered to the rat by application to the skin (*8*). Studies of the thiol content of the urine and other observations suggest that little of the S^{35} in the urine of rats dosed with radioactive BAL is in the form of unchanged BAL (*5*).

The work described above was supported by grants from the Directorate of Chemical Warfare, Department of National Defence, Ottawa, Canada. Grateful acknowledgment is made to the Director of Chemical Warfare for permission to publish the present article.

References[1]

1. Berenbom, M. Unreported observations.
2. Manson, L. A., Zbarsky, S. H., and Young, L. Report C.P. 85, 1945.
3. Peters, R. A., Stocken, L. A., and Thompson, R. H. S. *Nature, Lond.*, 1945, **156**, 616.
4. Simpson, S. D. Report C.P. 48, 1944.
5. Simpson, S. D. Unreported observations.
6. Simpson, S. D., and Young, L. Report C.P. 49, 1944.
7. Simpson, S. D., and Young, L. Report C.P. 79, 1945.
8. Simpson, S. D., and Young, L. Report C.P. 80, 1945.
9. Simpson, S. D., and Young, L. Report C.P. 84, 1945.
10. Simpson, S. D., Zbarsky, S. H., and Young, L. Report C.P. 63, 1944.
11. Waters, L. L., and Stock, C. *Science*, 1945, **102**, 601.
12. Young, L. Progress Report No. 21, 1942.
13. Zbarsky, S. H. Unreported observations.
14. Zbarsky, S. H., Manson, L. A., and Young, L. Report C.P. 72, 1944.
15. Zbarsky, S. H., Simpson, S. D., and Young, L. Report C.P. 64, 1944.

[1] The reports to which reference is made were submitted to the Director of Chemical Warfare, Department of National Defence, Ottawa, Canada.

Technical Papers

Thiamine Deficiency and High Estrogen Findings in Uterine Cancer and in Menorrhagia [1]

J. Ernest Ayre and W. A. G. Bauld

Gyne-cytology Laboratory, Royal Victoria Hospital
McGill University, Montreal

While studying vaginal and cervical cytology smears for a diagnosis of uterine cancer, the observation was made that over two-thirds of the 150 cases proven to be cancer showed evidence of abnormally high endogenous estrogenic activity. This observation assumed a greater significance when postmenopausal cases of 60 and 70 years of age manifested a cytology picture of estrogenic cornification similar to that of a young woman in the regenerative phase of the sex cycle.

The quantitative production, metabolism, and excretion of the estrogens is even today obscure. Blood assays have proven unsatisfactory, and urinary levels are a measure of the excretion but not of the endogenous level. Our studies lead us to believe that perhaps the simplest and most sensitive measure of endogenous estrin at our disposal today is the specific hormonal cornification reaction manifested in the cells of the squamous epithelium of the vagina.

In humans and in monkeys the estrogens manifest their presence in the vaginal mucosa by a cornification change in the cells, first described by Allen (*1*), which is accompanied by proliferation of the vaginal and cervical squamous epithelium. This growth change is related to the deposition of glycogen in the squamous cell, which is mediated and controlled by the force of the estrogenic stimulus. The vaginal epithelium of the average postmenopausal female is made up largely of basal cells which contain no glycogen, and cornification is absent. Under the influence of the estrogenic hormone the deposition of glycogen may be brought about, and cornification of the squamous cells occurs whether the subject be postclimacteric or following oöphorectomy. This was demonstrated in monkeys by Robertson, Maddux, and Allen (*17*), and in humans by Krumm (*13*). We have confirmed the latter's observations in our own laboratory. We have found further confirmation of the estrogenic activity by studying the endometrium of senile patients suffering from cancer of the cervix. Many of those showing cornification in the smears also exhibited endometrium identical to that found in an active regenerative phase, while in other cases the estrogenic stimulus was sufficient to produce a picture of glandular hyperplasia.

The findings of various investigators using laboratory animals would appear to indicate that liver damage may be induced by dietary deficiency which results in interference with estrogen inactivation. Biskind and Biskind (*3*) demonstrated that in female rats the liver loses its ability to inactivate estrogen in vitamin B-complex deficiency. Addition of brewer's yeast to the diet was found to restore the inactivating mechanism (*5*). The amount of estrogen inactivated by the liver could be controlled at will by withholding the vitamin B complex or by restoring it to the diet.

Singher and his associates (*18*) have demonstrated that thiamine and riboflavin are essential in the metabolism of estradiol by liver slices. The inactivation of estradiol is dependent upon the concentration of these vitamins in the liver, and they state that it seems possible that these vitamins may be involved in estrogen metabolism through their role as members of an oxidative enzyme system.

It has been recognized that menorrhagia and metrorrhagia may occur early in the course of cirrhosis of the liver (*12*), and the work of György and Goldblatt (*9*) and of others has demonstrated that cirrhosis of the liver is known to result from nutritional deficiency. Sources of the B complex have been shown to protect the liver against a variety of toxic agents such as lead, arsenic, and dimethylaniloazobenzene, which cause functional and morphologic damage to this organ. In addition to this evidence, Goldberger (*8*) has shown that menorrhagia may occur in pellagra.

Pincus and Graubard (*15*), in studying estrogen metabolism in seven women suffering from cancer of the uterus, concluded that these cases metabolized the estrogen in an abnormal manner. Their most striking finding was that the total estrogen urinary output after estrone and progesterone administration showed only a slight or negligible increase. The fact that the estrogen could not be accounted for might be explained on the basis of a liver block.

In treating women suffering from menorrhagia, metrorrhagia, and other disorders with large doses of B complex and liver extract, the Biskinds (*4*) report

[1] This work aided by a grant from the Ortho Research Foundation. The authors wish to express appreciation to Drs. J. R. Fraser, N. W. Philpott, and J. S. L. Browne for valuable advice and cooperation in the preparation of the work; to the Nutrition Laboratory of the McGill University Clinic; and to Drs. W. Andreae and M. Hoffman for their assistance and advice in regard to the thiamine levels and liver function tests, respectively.

Acknowledgment with thanks is made to the following companies for the supplies of vitamin B_1 and B complex used during the course of this investigation: Lederle Laboratories, Inc., New York City; Winthrop Chemical Company, Windsor, Ontario; Ayerst, McKenna and Harrison, Montreal; E. R. Squibb and Sons, New York City; Charles E. Frosst and Company, Montreal; and Frank W. Horner, Ltd., Montreal.

correction of the functional disorders in a high percentage of cases.

For the past year we have studied 180 ambulatory gynecologic cases suffering from menorrhagia or amenorrhoea. While these patients were not accessible for biochemical assays, it was found possible to add to the clinical findings the simple estrogen determination in the cytology smears before and after administration of thiamine chloride and the other constituents of the B complex and liver extract. While these studies have not been published or completed as yet, one salient feature has been noted, viz., that some definite relationship exists between the intake of B complex and the rise and fall of the estrogenic levels in the body as manifested by the cornification counts in the vaginal smear. Clinically, uniform improvement has been shown in cases other than those proven to have an inflammatory etiology, and the cytology smear findings have given us additional laboratory evidence to help explain why improvement occurred. In some cases we have found a dramatic drop in the cornification level after administration of B complex, as if some part of this preparation were acting specifically in the elimination of the estrogen. It is regrettable that urinary estrogenic levels were not followed at the same time. One might expect that if a block were actually present in the liver, the blood levels and the vaginal cornification would be high and the urine levels low. Coinciding with a drop in the cornification level subsequent to B-complex administration, the urinary estrogen should increase. (Further cases are being studied with a view to verifying this.) Also, the evidence would be more complete if liver function tests were available to assess damage such as might interfere with elimination of the estrogens.

Whether or not the accumulation of uncertain quantities of various estrogens in the body would act as a carcinogen to the susceptible Mullerian tissues and the glands of the breast is open to question. It is known that estrogen is essentially a growth-promoting hormone acting most specifically on the endometrium, which, during each monthly cycle, undergoes the most rapid growth occurring physiologically in the body. Its effect is also specifically exerted upon the squamous epithelium of the vagina. But this same type of epithelium covers the cervix, shows the same cyclic growth changes, and is the tissue most commonly involved in malignancy in the human female.

The role of the estrogens in inducing proliferation of the vaginal epithelium was described in castrate monkeys by Allen (*2*) and has since been confirmed in humans by Shorr and others (*6*). As a result of the injection of estrogens an enormous growth in the vaginal epithelium can be induced, associated with an increase in the number of growing bulbs alon the basement membrane, the cells of which conta many mitotic figures. Allen has cautioned that t increased incidence of malignant change followi administration of estrogens to cancer-susceptib strains of animals must serve as a warning to t potentialities in the human. While the short life-cy of mice permits an early recognition of what is ca cinogenic, the same influence acting upon human t sues during the same fraction of a lifetime mig produce a malignant growth in man. Therefore, seems possible that errors of diet leading to persiste or intermittent deficiency of such elements as thiami might cause a persistent estrogenic growth stimul tion over a period of years which, acting upon a "loc minoris resistentiae" such as an erosion, ultimate produces a malignant neoplasm.

From our own experiences we may recall cas where we must incriminate an estrogen in the develo ment of cancer. The development of carcinoma in t breast following weekly injections of an estrog for menopausal therapy is in itself inconclusive e dence. But when such cases occur time and agai they assume greater significance. Dr. J. S. Hen (*10*) has reported two cases in whom the administr tion of stilbestrol over a period of many months w followed by the finding of malignant growths in t uterus.

It has been found that the implantation of ovari tissues into mice produced cancer of the breast cancer-susceptible animals, and it was thought fr this that some secretion of the ovary played a role the production of cancer. It has long been recogni that certain coal tar products produce cancer w greater certainty than any other known chemical physical irritant. The chemical structure of t responsible substance has been found to be simi to that of some of the active substances in the hormones.

Rhoads (*16*) has presented evidence to show t in rats the administration of one of these two-benz ring substances, "butter yellow," will result in development of cancer when their diet consisted polished rice and carrots. If liver or yeast was ad to the basal diet, no cancer occurred. Here, clea was an experiment in which a dietary constituent, in its content of the vitamins of the B complex, protective against induced cancer.

A recent survey of evidence of estrogenic acti in 62 granulosa cell tumors has been made by H son, Dockerty, and Mussey (*11*). They stated "evidence of hyperestrinism is afforded in our se by symptoms of precocious puberty, amenorrh and post menopausal bleeding." They reported liferative endometrium in 67 per cent of their c

38 postmenopausal patients who had granulosa l tumor they reported 21 per cent as showing an dependent endometrial carcinoma, and in one-third these cases carcinoma of the breast with axillary etastasis also developed. They concluded that "this enomenon of co-existent ovarian, endometrial and mmary carcinoma in the human being bears a rked similarity to the results of experiments on oratory animals in which estrogen stimulation ap- ars to be a factor in carcinogenesis."

During the course of making routine cytological dies on some of our gynecologic bleeders, three cases re encountered in whom similar cytology findings ompted us to investigate the nutritional biochemical tus of these patients.

The three cases were 14, 29, and 64 years of age, spectively. The first was suffering from pubertal eding which followed a total dental extraction. e other two showed evidence of malignancy in cytol- y smears, as described so expertly by Papanicolaou d Traut (*14*). All were bleeding excessively, and showed abnormally high estrogen levels in the tology smears as well as thiamine deficiency when eir urinary excretion levels were analyzed by Dr. ndreae, of the Nutrition Department of the McGill iversity Clinic.

In the present investigation the vitamin status was timated by a vitamin-tolerance technique. Follow- g a vitamin-free supper the urine from 12:00 mid- ght to 8:00 A.M. was collected in a bottle contain- g acetic acid. In the morning, after a vitamin-free eakfast, an intramuscular injection of 1 mg. thia- ine and 1 mg. riboflavin was given and the urine llected for the subsequent four-hour period. Both ecimens were analyzed—by the thiochrome method Wang and Harris (1943) (*19*) for thiamine, and the Ferrebee (*7*) method (1940) for riboflavin. tients with below-normal excretion values were lassed as deficient in thiamine and/or riboflavin.

The other vitamin B factors measured were normal amount. Liver function tests were taken on all es with uncertain results. The first case showed prolonged prothrombin time, and the second an normal cephalin flocculation test (plus 2 in 24 and 8 hours), while the third showed a bromsulfalein tention of 10 per cent. Dr. M. Hoffman, who has udied liver function tests intensively, states that no ingle test has as yet been elaborated to assess liver amage, and it is possible to have liver damage suffi- ient to interfere with estrogen elimination without damage being detectable by the tests at present our disposal.

The endometrial patterns in these cases verified the igh estrogen levels shown by cytology counts. In the two cases varying degrees of active hyperplasia were found. An endometrial biopsy was not obtained in the third case.

The most striking feature, however, was the evidence of growth manifestations in the 29-year-old case, who exhibited most unusual evidence of proliferation in the squamous tissues of the cervix. Cytology smears taken from the cervix and vagina showed many cornified cells, but in addition there were many immature and anaplastic squamous cells with huge nuclei showing numerous chromatin bundles. Atypical cells were found showing all grades of variability from the normal basal cell to the most bizarre malignant type of cell with the nuclear heteroplasia characteristic of cancer. These findings appear the more remarkable in that no cancer was visible clinically—only a suspicious-appearing erosion encircling the external cervical os. Following surgery, the lesion from which these cells had become desquamated was located. Pathological study left an element of question, however, when one pathologist diagnosed a squamous intraepithelial carcinoma, while another diagnosed it as "precancerous secondary hyperplasia" of the cervix.

The tissue study in the case of the 14-year-old case of pubertal bleeding proved interesting also. Grossly, the tissue was thick, abundant, and polypoidal, while microscopically, various areas presented an appearance of overstimulated proliferative glands with mitosis and adenomatous formation such as would make the pathologist think twice before eliminating a diagnosis of precancerous change if found in a 40-year-old. Yet such a diagnosis would seem fantastic in a child of 14 years!

The third case exhibited a typical squamous carcinoma of the cervix, an early small lesion, but a rapidly growing undifferentiated neoplasm.

One might readily expect that a cancerous victim in the throes of cachexia might show justification for deficiency, but investigation into the dietary intake reveals that in the two cases of neoplasm, the lesions were early and asymptomatic except for the bleeding. The 29-year-old case was suffering from chronic constipation, abdominal cramps, and nausea brought on by solid food, which restricted her to a liquid or soft diet. In addition, she was a moderately heavy drinker.

The other case revealed excellent nutrition externally, but she admitted that she dieted constantly to keep her weight down, and analysis of her diet revealed an inadequate thiamine intake.

Nutritional Studies

It perhaps seems remarkable in these days of scientific enlightenment and dietary refinement that deficiency would occur irrespective of the economic status of the patient. It has long been a general

feeling among gynecologists that dietetics were not directly concerned with the production of pelvic pathology, and that the need for vitamins in particular was generally overstressed. It would seem logical that the average person with a normal appetite for the various staple foods should not develop a deficiency due to an inadequate intake. A study of thiamine physiology and metabolism reveals evidence to indicate that this substance would appear to be particularly vulnerable to intermittent or chronic depletion without gross deficiency in the diet as a whole. This tendency would appear to depend upon the fact that little thiamine is stored in the organism and the amount is sufficient only to maintain proper life for a few days. A daily intake of thiamine is necessary, and the organism absorbs only enough for the immediate needs, the excess being destroyed or excreted. More is required when alcohol is imbibed or when a high carbohydrate diet is taken. Fats, on the other hand, spare thiamine. This may account for the finding of deficient levels in well-nourished but obese patients who are constantly dieting. We have found that a vicious cycle may occur, as anorexia and constipation frequently develop in the presence of a deficiency. Therefore, the greater the anorexia the more pronounced the deficiency.

With so much discussion of vitamin therapy nowadays, one might be led to believe that they are a "cure-all." The truth, however, is that vitamins are only nutritional elements, and to say that a vitamin would cure a deficiency or a disease resulting from a deficiency is simply to say that a well-balanced diet, properly absorbed and utilized, would have prevented the disorder.

After observing the consistency of finding "B" deficiency in so many gynecologic cases, one naturally wonders if half the population may be deficient. If so, the reported findings would lose much of their significance. But this is not the case. Dr. Andreae reports that of the cases in the Royal Victoria Hospital tested because of a suspected deficiency, only one in eight has been proven to be deficient. Further, our own controls of nongynecologic cases reflect the same normalcy.

Speculation arising from an analysis of the findings in the cases herein presented suggests the inference that the thiamine deficiency was causally related to the pathological conditions found. A possible mechanism to explain functional bleeding and the development of a malignant growth in the estrogen-susceptible pelvic tissues presents itself. Is it possible that the dietary deficiency, acute in the case of pubertal bleeding, and chronic in the two cases of cancer, produced some barely demonstrable liver damage which was sufficient to inhibit this organ from conjugating the estrogens necessary to permit their inactivation? Is it possible that the accumulation of the estrogenic substances produced the overgrowth of the endometrium, resulting in endometrial hyperplasia with its characteristic bleeding? And is it possible that as a result of such liver damage the estrogen accumulating in the system, unable to escape, continually exerting its growth stimulation upon the pelvic tissues over a period of years, leads to an actual carcinoma?

Summary

The finding of abnormal estrogenic activity coupled with thiamine deficiency in cases of menorrhagia and uterine cancer suggests a possible etiological correlation between the dietary deficiency, the abnormal estrogen level, and the pathological lesion.

The specific element deficient in these cases was thiamine, while the other B factors were normal.

Preliminary report of the evidence is made in this small series while more extensive studies on a large series of cases are being pursued.

Cornification in cytology smears was used to study estrogenic activity, since the present study was prompted by cytological findings; the method is simple, practical, and reasonably accurate. The urinary estimation measures only the amount excreted, and if liver impairment actually is present, the quantity excreted would not give a true index of the amount retained in the body.

Further studies are being undertaken in which estrogenic, urinary, and cornification levels are being compared before and after thiamine administration in cases proven to be deficient.

Supplement. Since the original submission of this paper, further cases have been investigated. Of 20 cases suffering from proven uterine cancer, 90 per cent of these were found to have a low thiamine excretion coupled with an abnormally high endogenous estrogen level. The average thiamine excretion level was found to be less than half the average levels found in a control group which showed normal estrogen levels.

Of the 20 cancer cases studied, 20 per cent showed also a deficient excretion of riboflavin.

A similar group of menorrhagic patients was studied and showed the same co-relation of thiamine deficiency and an abnormally high estrogenic level.

In an attempt to explain why some cases develop menorrhagia and others cancer, the time element may enter the picture. Since most people develop a fixed habit of diet, a dietary error over a period of time would tend to produce a chronic deficiency. If this acts on the human liver in the same way as in animals,

would seem logical that even small amounts of trin, not being inactivated by the liver would accumulate in the body and at the same time act as a ronic growth stimulant to the estrin-susceptible ssues, viz., the pelvic organs and possibly also the lands of the breast.

The fact that dietary errors tend to be chronic is own in certain of our cancer cases, where even after ure, or a remission of months or years, they return the same habits of diet and continue to show thiaine deficiency. While we must also consider the ossibility of an internal metabolic defect leading to e deficiency, this would tend to be countered by e fact that with correction of dietary intake the eficiency was corrected in our cases. Whether or ot these cases require an increased quantitative inake of these essentials to maintain a normal level emains to be investigated.

Conclusions

When we couple the findings with the background of what has been proven in animals, there appears to be excellent circumstantial evidence to suggest that the nutritional deficiency may have been a primary factor leading to the malignancy.

Whether this low thiamine excretion is due to an actual primary dietary deficiency or to some internal metabolic change is a subject for further investigation. In either case, if this hypothetical mechanism proves to be correct, it means that we are presented with the means not only of diagnosing uterine cancer by cytological findings but of actually detecting a potential cancer-producing mechanism even before the cancer develops! Two simple tests would be used: (1) a cervical cytology test, which would tell (a) if the person had uterine cancer, and (b) if not, whether the endogenous estrogen level was abnormally high, in which case the second test should be done; and (2) a test of the urinary thiamine level.

The finding of a combination of low thiamine and abnormally high estrogen could be recognized as a dangerous precancerous linkage. Recognition of this would permit correction and possible prevention of the cancer.

No single track of investigation yields a conclusive answer to the cancer enigma, but when we piece together the evidence of animal experimentation, cytopathological, hormonal, and nutritional findings, there seems to be evidence that progress in the right direction is being made.

References

1. Allen, E. *Amer. J. Anat.*, 1924, **34**, 133.
2. Allen, E. *J. Amer. med. Ass.*, 1935, **104**, 1496.
3. Biskind, M. S., and Biskind, G. R. *Endocrinology*, 1942, **31**, 109.
4. Biskind, M. S., Biskind, G. R., and Biskind, L. H. *Surg. Gynec. Obstet.*, 1944, **78**, 49.
5. Biskind, M. S., and Shelesnyak, M. C. *Endocrinology*, 1942, **30**, 819.
6. DeAllende, Ines, L. C., Shorr, Ephraim, and Hartman, Carl G. In *Contributions to embryology. Carnegie Inst. Publ. 557*, 1943, **32**, 1–26.
7. Ferrebee, J. W. *J. clin. Invest.*, 1940, **19**, 251.
8. Goldberger, J. Tice's *Practice of medicine.* (Rev. by W. H. Sebrell.) Vol. 9, 1932, p. 205.
9. György, P., and Goldblatt, H. *J. exp. Med.*, 1942, **75**, 355.
10. Henry, J. S. *Canad. med. Ass. J.*, 1945, **53**, 31.
11. Hodgson, J. E., Dockerty, M. B., and Mussey, R. D. *Surg. Gynec. Obstet.*, 1945, **81**, 631–642.
12. Kelly, A. O. J. *Osler's mod. Med.*, 1908, **5**, 775.
13. Krumm, J. F. *Amer. J. Obstet. Gynec.*, 1936, **31**, 1035.
14. Papanicolaou, G. N., and Traut, H. F. *Amer. J. Obstet. Gynec.*, 1941, **42**, 193.
15. Pincus, G., and Graubard, M. *Endocrinology*, 1940, **26**, 430.
16. Rhoads, C. P. *Bull. N. Y. Acad. Med.*, 1942, **18**, 53.
17. Robertson, D. C., Maddux, W. P., and Allen, E. *Endocrinology*, 1930, **13**, 77.
18. Singher, H. O., Kensler, C. J., Taylor, H. C., Jr., Rhoads, C. P., and Unna, Klaus. *J. biol. Chem.*, 1944, **154**, 79.
19. Wang, Y. L., and Harris, L. J. *Brit. med. J.*, 1943, 451.

The Antibacterial Activity of Protamine Zinc Insulin[1]

Carol Houck Bollenback and Sidney W. Fox

Chemistry Section, Iowa Agricultural Experiment Station, Ames

As part of a program of chemical and biological study of proteinaceous antibacterials (*3*), it seemed desirable to test the effect of protamine insulin combinations of the kind used routinely in the control of diabetes (*1*). The antibacterial property of the protamines, clupein (*5*), and salmine (*7*), had previously been reported. Protamine sulfate prepared from shad of the Sacramento River by one of us (S.W.F.) has also been found to possess comparable activity (*2*). The experiments recorded below indicate that protamine is able to act as an antibacterial, even though combined in a relatively insoluble form with insulin.

The tests were conducted on cultures of *Lactobacillus arabinosus, Staphylococcus aureus,* and *Escherichia coli.* Both the supernatant liquid of centrifuged protamine zinc insulin preparations and the whole suspension, with appropriate controls, were tested. All tests were run in solutions buffered by phosphate. The contents of the tubes were initially at pH 7.1–7.4. *Lactobacillus arabinosus* was cultured at 30° in the special Bacto-Peptone medium of McMahan and Snell (*6*) and in the synthetic medium of Kuiken, *et al.* (*4*). The other two organisms were cultured at 37° in the usual beef extract broth. The observations recorded in Table 1 were made at 24 hours from tube cultures. All results were confirmed by plate cultures read at 48 hours. These plate cultures were made from well-shaken suspensions after an initial growth in

[1] Journal Paper No. J–1288 of the Iowa Agricultural Experiment Station, Project 897, in cooperation with the Veterinary Research Institute.

tubes for 24 hours. In order to test the possibility that the cells are prevented from proliferating because of engulfment within the solid, shake cultures were

TABLE 1

LOWEST DILUTIONS OF PROTAMINE AND INSULIN PREPARATIONS PERMITTING GROWTH IN SEVERAL SPECIES OF BACTERIA

Microorganism	Protamine zinc insulin suspension	Protamine zinc insulin supernatant solution	Salmine	Zinc insulin
L. arabinosus on Bacto-Peptone medium	1/20,000	N.I.*	1/85,000	N.I.
L. arabinosus on synthetic medium	1/40,000	N.I.	1/200,000	N.I.
Staph. aureus Heatley	1/20,000	N.I.	1/50,000	N.I.
E. coli	1/10,000	N.I.	1/25,000	N.I.

* N.I. signifies no inhibition by the undiluted solution. The undiluted solution of zinc insulin contained 1.8 mg. of zinc insulin powder (Lilly) per cc. Dilution figures in the table refer to the fraction: weight of substance tested/weight of solution tested.

run on *Lactobacillus arabinosus* with a suspension of protamine zinc insulin at a concentration that was close to the threshold value in tubes. Results comparable to those for cultures in tubes were obtained.

Effective concentrations were determined by testing successive twofold dilutions of the original solution or suspension. All solutions were sterilized by Seitz filtration, and all mixtures were aseptically prepared from such solutions. The protamine zinc insulin preparation was obtained from commercial ampoules. The zinc insulin powder and salmine sulfate were the gifts of Mr. George Walden, of Eli Lilly and Company, to whom our thanks are expressed.

The phenol used as a preservative in protamine zinc insulin preparations contributes but slightly to its antibacterial activity. The data in Table 1 indicate inappreciable antibacterial activity for the supernatant liquid of centrifuged preparations. Substantially the same antibacterial activity was recorded for protamine zinc insulin suspensions prepared in this laboratory without the inclusion of any added preservative. The observed antibacterial effects are therefore not attributable to the phenol found in commercial preparations.

The activity of protamine zinc insulin appears to be approximately equivalent to the activity of the contained protamine (3.5 parts of protamine zinc insulin contain 1.25 parts of protamine). It seems reasonable to conclude, therefore, that the salmine zinc insulin dissociates to liberate salmine. This behavior is comparable to the gradual release of insulin for its regulated action when administered in insoluble complex form with protamine.

These observations indicate that there may be a previously unrecognized medical utility in the inclusion of protamine in insulin preparations.

References

1. AMERICAN MEDICAL ASSOCIATION. *New and non-official remedies*, 1944, 431.
2. FOX, S. W., BOLLENBACK, C. H., and FLING, M. Unpublished experiments.
3. FOX, S. W., FLING, M., and BOLLENBACK, G. N. *J. biol. Chem.*, 1944, **155**, 465.
4. KUIKEN, K. A., NORMAN, W. H., LYMAN, C. M., HALE, F., and BLOTTER, L. *J. biol. Chem.*, 1943, **151**, 616.
5. MCCLEAN, D. *J. Path. Bact.*, 1931, **34**, 459.
6. MCMAHAN, J. R., and SNELL, E. E. *J. biol. Chem.*, 1944, **152**, 84.
7. MILLER, B. F., ABRAMS, R., DORFMAN, A., and KLEIN, M. *Science*, 1942, **96**, 428.

Scanning Science—

Almost the only power clearly and expressly vested in Congress by the Constitution which has remained practically unexercised to the present day is that of fixing the standard of weights and measures. For more than a generation we lived with no legal standard by which could be determined even the amount of metal which went into the coin that came from our mints. Gallatin procured from France a platinum kilogram and meter in 1821 and from England a troy pound in 1827, and in 1828 the latter was recognized as the standard for mint purposes. In 1830 the Senate directed the Secretary of the Treasury to have a comparison made of the standards of weight and measure used at the principal custom houses of the United States and report the same to the Senate. This was done, and large discrepancies and errors were found to exist. Varying scales and varying measures inevitably produced varying rates of duty. The Treasury Department, therefore, in the exercise of its executive power and as a necessary incident and means to the execution of the law and the observance of the Constitution, adopted for the use of that Department the Troughton scale, then in the possession and use of the Coast Survey, as the unit of length, and the troy pound of the mint as the unit of weight. From the latter the avoirdupois pound was to be derived, assuming that they were 7,000 grains in the pound avoirdupois to 5,760 in the pound troy. By the Act of March 3, 1881, similar sets of standards were directed to be supplied to the various agricultural colleges which had received land grants from the United States at a cost not exceeding $200 for each set. This law was complied with as best it could be under the limitation of cost prescribed.

—27 March 1896

U. S. News and Notes

Capt. R. D. Conrad, USN, director of the Planning Division, Office of Research and Inventions, has been awarded the Legion of Merit. The award was made to Capt. Conrad for exceptionally meritorious services to the country in guiding research during the war years as planning head for the Office of the Coordinator of Research and Development. Rear Adm. H. G. Bowen, chief of Research and Inventions, made the award on behalf of Secretary Forrestal.

Dr. Merle A. Tuve, since 1938 chief physicist of the Department of Terrestrial Magnetism of the Carnegie Institution of Washington, has been appointed director of the Department of Terrestrial Magnetism, to succeed Dr. John A. Fleming. Announcement of the appointment was made on 26 March by Dr. Vannevar Bush, president of the Carnegie Institution. Dr. Fleming, a member of the Carnegie Institution's scientific staff since 1904 and director of the Department of Terrestrial Magnetism since 1935, will retire.

Dr. J. Allen Scott, of the University of Texas Medical School, who spent last summer in Brazil on a government health mission, recently addressed the Kansas State College Chapter of Sigma Xi on "Health Problems in the Amazon Valley."

Dr. D. H. Wenrich, of the University of Pennsylvania, will serve as acting editor of the *Journal of Morphology,* published by the Wistar Institute, until a new editor is appointed by the American Society of Zoologists. The vacancy was caused by the death, on 17 January 1946, of Dr. C. E. McClung, who served as managing editor for 25 years.

Lt. Col. Charles H. Greenall, director of research at Frankford Arsenal, has been named executive director of the Franklin Institute Laboratories, Philadelphia. Dr. Henry Butler Allen is secretary and director of the Institute.

Senior consultants to Dr. Allen will be Dr. Rupen Eksergain, of Media, chief consulting engineer for the Edward G. Budd Manufacturing Company, and Dr. W. F. G. Swann, of Swarthmore, director of the Bartol Research Foundation of the Franklin Institute on the campus of Swarthmore College.

Three other members of the administrative personnel named for the laboratories are Dr. Nicol H. Smith, director of the Division of Chemical Engineering and Physics, and Ralph H. McClarren, Division of Electronics and Instruments, both of whom are associate directors of the Institute museum; and George S. Heoll, Division of Mechanical Engineering.

Dr. J. Wyatt Durham has been made associate professor of invertebrate paleontology at California Institute of Technology. He will join the staff in August 1946.

Dr. Lee A. DuBridge, director of the NDRC Radiation Laboratory, Cambridge, returned to the University of Rochester on 15 February to resume his headship of the Department of Physics. At Cambridge Dr. DuBridge supervised the work of 3,900 people on a budget of some $4,000,000 a month.

Dr. Richard H. Jahns has been made assistant professor of geology at the California Institute of Technology.

Dr. Harold C. Urey, returned to his Alma Mater, Montana State University, as the principal speaker at a Charter Day celebration of the completion of 50 years existence of that institution. Dr. Urey spoke also at the Missoula County High School, at the annual meeting of the Missoula Chamber of Commerce, and before the University Sigma Xi Club.

Dr. Jackson W. Foster has resigned as head of the Microbiological Research and Development Department at Merck and Company, Inc., to accept an appointment as associate professor of bacteriology at the University of Texas, Austin.

Dr. Paul B. Sears, professor of botany and head of the Department of Botany at Oberlin College, has recently been appointed a member of the State Commission on Conservation and Natural Resources for the State of Ohio by Governor Frank J. Lausche.

Dr. Laurence H. Snyder, of the Ohio State University, addressed the New York Academy of Science on 11 February on the topic: "Recent Advances in Human Heredity."

Dr. Julius Ashkin, who was at Los Alamos for three years, has been appointed assistant professor of physics at the University of Rochester.

Cecil W. Mann has been promoted to a full professorship in psychology at the Tulane University of Louisiana.

G. W. Bergren, instructor in mechanical engineering at Purdue University, has returned to the University after four and a half years of service with the Navy.

Announcements

Dr. Arthur H. Compton, chancellor of Washington University, spoke at the luncheon at which the medals and scrolls were presented to 13 science writers as part of the George Westinghouse Science Writing Awards on Wednesday, 27 March, at St. Louis.

Dr. Compton pointed out that the rapid changes going on in the world are largely a result of scientific insight and technology based on scientific achievement. He paid tribute to the profession of science writing because it helps to keep people aware that it is science that is causing the day to day changes in the world. He observed that science writing for the general public is a steadying influence in a changing world because it helps people to anticipate changes in their lives before these changes are really upon them. This helps to make people feel at home in what would otherwise be a strange world. Dr. Compton also pointed out that science writers ". . . would do well to call more attention to the fact that a society which is based upon science is a society of specialists, and that specialists form a strong society only when cooperation is effective. This means that the growth of science implies a need for greater attention to understanding, tolerance, and coordination of effort between the various components that make up our society. We have found that science does not advance without dividing into specialties; society needs these specialties. Here, then, in a new sense is a need for cooperation if our society is to function. Prejudices and intolerances, whether between professions, or races, or economic groups, become a supreme social hazard. The desire to work together for the common good becomes the supreme virtue in a society of scientific specialists."

Ralph Coghlan, editor of the editorial page, *St. Louis Post-Dispatch,* also spoke in a humorous and intimate fashion, pointing out that although the press has so often mutilated scientific theory, misrepresented it, and often unduly raised the hopes of people by prematurely announcing cures of deadly diseases, scientists themselves are responsible for this state of affairs, having lived too long in ivory towers and enjoyed to the full their intellectual snobbery.

Dr. Anton Carlson presented the medals, saying that, however good science writing is now, much remains to be done, as witnessed by scientifically stupid, ignorant actions on the part of the public.

A Microbiological Section of the Botanical Society of America, Inc., was established at the St. Louis meeting of the Society. The Microbiological Section will be comprehensive in scope and organization and includes mycologists, plant physiologists and biochemists interested in microorganisms, pathologists, algologists, protozoologists, bacteriologists, medical mycologists, and students of antibiotics. It will, accordingly, provide the organization and outlet for publication for research workers on microorganisms.

Following organization of the Microbiological Section at St. Louis, a program on microbiology was presented on the afternoon of 28 March. Dr. Paul R. Burkholder, of Yale University, and Dr. Kenneth B. Raper, of the Northern Regional Research Laboratory, Peoria, Illinois, were elected chairman and secretary, respectively, of the Microbiological Section. The new Section was organized in view of the growing importance of microorganisms in the production of antibiotics and in general botanical, bacteriological, and industrial research.

The Editorial Board of the American Journal of Botany announces the election of Prof. Bernard S. Meyer as editor-in-chief to succeed Dr. Ralph E. Cleland. Dr. Meyer assumed his duties on 22 March. All manuscripts and correspondence relating to editorial matters should be addressed to Prof. Bernard S. Meyer, Botany Department, Ohio State University, Columbus 10, Ohio.

The Central Institute for the Deaf in St. Louis and the Harvard University Psycho-Acoustic and Electro-Acoustic Laboratories, operating under OSRD, have devised new methods of testing the degree of deafness of returning veterans with impaired hearing. All of the currently approved commercial hearing aids, 14 in number, were tested.

With the assistance of conscientious objectors and of volunteers who are themselves hard of hearing, tests were conducted over a period of two years to find out more about how the partially deafened ear really works and to measure the loudest sound which both the normal and deafened subject can tolerate with comfort.

Differences in the performance among hearing aids proved to be much less than had been anticipated, but since hearing aids are devices to which persons become accustomed, individual preferences do have to be reckoned with.

The scientific program, known as the Hearing-Aid Project, was established with the assistance of Col. M. R. Mobley, later awarded the Legion of Merit, in close liaison with military hospitals where soldiers and sailors with impaired hearing were diagnosed and fitted with hearing aids.

The Central Institute for the Deaf planned and assembled equipment for military hospitals, suitable for testing impairment of hearing and selection of the hearing aid best suited to each patient.

Apparatus for the tests were installed at the Deshon General Hospital, Butler, Pennsylvania; the Borden General Hospital, Chickasha, Oklahoma; the Hoff General Hospital, Santa Barbara, California; and the U. S. Naval Hospital, Philadelphia, Pennsylvania.

New methods of testing developed at Harvard's Psycho-Acoustic Laboratory under direction of Hallowell Davis, associate professor of physiology, who now has become the new research director of the Central Institute for the Deaf, are based on the ability to hear and understand speech. They supplement the familiar test of hearing by the audiometer, which employs relatively pure tones.

By these new methods, carefully chosen lists of words or sentences are delivered by earphones or loudspeaker in an acoustically treated, sound-proof room. Loudness is measured and regulated electrically. Tests have been standardized by the use of phonographic recordings or by training technicians to speak in standard manner into a microphone. A standard noise can be added electrically if desired.

To provide basic information for the design of hearing aids, the Central Institute for the Deaf determined the limits of tolerance for normal and for hard-of-hearing ears.

It has been suggested in recent years that a hearing aid should fit, *i.e.* compensate in detail for each patient's individual hearing loss, much as a pair of eyeglasses is prepared by individual prescription. In these experiments, however, for all types of hearing loss, better results were obtained with an instrument which provided high fidelity amplification over an adequate range of frequencies rather than selective amplification. The ideal hearing aid should deliver speech at the maximum necessary loudness with a minimum of distortion.

Six graduate teaching and research assistantships are offered by the Department of Zoology of the Graduate School and the College of Liberal Arts of Syracuse University. The duties consist of half-time work largely in undergraduate teaching, and in some cases in assisting in experimental research projects. It is expected that the remaining portion of the student's time will be spent in graduate study in the Department of Zoology and allied departments leading to the M.A. degree (two years) or Ph.D. Thesis work leading to advanced degrees may be taken in the following fields: invertebrate zoology, vertebrate zoology, general physiology, vertebrate physiology, endocrinology, cytology, protobiology, and parasitology.

These appointments, open to graduates with high scholastic records from any accredited university or college, are made for two terms during the year 1946–47. The assistantships carry a stipend of $1,000 each for the year except in the case of veterans qualifying under the G. I. Bill of Rights, who will receive $800, since tuition in these cases is provided by the Government. Assistance during the summer term or summer session carries an extra stipend.

Application blanks may be obtained from: Dr. R. D. Manwell, secretary, Department of Zoology, Lyman Hall, Syracuse University, Syrause 10, New York.

Formation of the Soil Conservation Society of America, a professional organization for workers in that and allied fields, is announced by J. H. Christ, of Portland, Oregon, national secretary-treasurer. Ralph H. Musser, of Milwaukee, Wisconsin, is president of the society that enrolled 1,500 members in 1945, the year it began to function. A. E. McClymonds, of Lincoln, Nebraska, is vice-president.

The society was organized to "promote and advance all phases of the science of conservation of soil and water resources; to provide a medium for exchange of facts, experience, and thought; and to present, advance, and protect the standards of the science of soil and water conservation." Dr. Hugh H. Bennett, of Washington, D. C., chief of the Soil Conservation Service of the U. S. Department of Agriculture, is founder of the society.

Plans have been made to publish a quarterly journal, beginning in the last half of 1946. The annual dues are $3.00; the address of the secretary-treasurer, P. O. Box 671, Portland 7, Oregon.

The following statement was unanimously adopted at a membership meeting of the Philadelphia Branch of the American Association of Scientific Workers, 2303 Delancey Place, Philadelphia 3, Pennsylvania, on 28 February 1946:

The current spy scare confirms the repeated contention that surrounding atomic energy in a veil of secrecy hampers freedom of research and even threatens world peace.

Scientists have repeatedly emphasized that atomic research cannot be kept secret. However, the illusion of secrecy that prevails at this time inevitably produces an atmosphere of intrigue, rumor-mongering, and distrust among nations. Thus, the Canadian accusations, magnified by the press, have alarmingly strained normal relations between Canada and the Soviet Union. Critical incidents of this sort will continue until all the facts about the making of atom bombs are in the hands of the Security Council of the UNO, where this knowledge can be used by all nations harmoniously, in the interest of peace.

Scientists particularly should note the fact that members of the National Research Council of Canada were among those accused in the spy episode. One is made aware that no laboratory will be inviolate if hysteria about "atomic secrets" is allowed free rein. This

danger was dramatically brought home to us in America when General Groves made the outrageous charge that "atomic secrets" had leaked out through the testimony of scientists favoring the McMahon Bill, which provides for civilian control of atomic research. Scientists resent this slur on their integrity and will fight any attempt to intimidate them and prevent them from taking their rightful place in the discussion on control of atomic energy.

We suggest that scientists, and others who are concerned to see the discovery of atomic energy perverted into channels which hinder progress rather than furthering it, do the following:

1. Write President Truman and Secretary of State Byrnes urging that international tensions surrounding the question of the use of atomic power be ended by the *immediate* turning over of all information on the subject to the Security Council of the UNO.

2. Write Senator McMahon in support of his bill, S. 1717, because it would allow the freest expansion of research in nuclear physics.

The four hundred fourteenth meeting of the American Mathematical Society was held at Columbia University on Saturday, 23 February 1946.

The Association for Symbolic Logic also met on 23 February 1946 at Columbia University.

Meetings

The National Academy of Sciences will hold its annual meeting on 22, 23, and 24 April in Washington, D. C. Sessions for the presentation of invited scientific papers will be held in the auditorium of the New National Museum and will be open to the public. The program follows:

Monday, 10:00 A.M.–12:30 P.M.—"Establishment and Activities of USN Medical Research Unit No. 2 in the Pacific": T. M. Rivers, Rockefeller Institute for Medical Research; "Antimalaria Compounds": C. S. Marvel, University of Illinois; "The Study of the Antimalarial Activity in the Human": J. S. Shannon, Goldwater Memorial Hospital; "Antibiotics With Special Reference to Streptomycin": S. A. Waksman, Agricultural Experiment Station, New Brunswick; "Penicillin and Syphilis": J. E. Moore, Johns Hopkins University; "Insecticidal Action and Chemical Composition of Organic Compounds": A. L. Haller, U. S. Department of Agriculture; "Submarine Propagation of Sound Waves": M. E. Ewing, Columbia University.

Monday, 2:00 P.M.–5:00 P.M.—"Screening and Toxic Smokes": W. H. Rodebush, University of Illinois; "Catalytic Cracking of Petroleum Oils": W. K. Lewis, Massachusetts Institute of Technology; "Chemistry in Germany Today": Roger Adams, University of Illinois; "Explosives in World War II": C. B. Kistiakowsky, Harvard University; "The Mechanism of the Emulsion Polymerization of Rubber and Other Polymers": W. D. Harkins, University of Chicago; "Recent Developments in Meteorological Equipment": A. F. Spilhaus, New York University; "Waves and Vortices in the Atmosphere": J. Bjerknes, University of California, Los Angeles; "Progress in the AAF Toward the Development of a Science of the Use of Human Resources": Col. J. C. Flanagan, AAF; "Inequalities in Adult Capacity—From Military Data": W. V. Bingham, War Department.

Monday, 8:30 P.M.—"Science in the Framework of International Policy": Isaiah Bowman, president, Johns Hopkins University.

Tuesday, 10:00 A.M.–12:30 P.M.—"Jet Propulsion": J. C. Hunsaker, Massachusetts Institute of Technology; "Some Recent Advances in Aerodynamics": H. L. Dryden, National Bureau of Standards; "The Radio Proximity Fuse": M. A. Tuve, Carnegie Institution of Washington; "Microwave Radar": L. A. DuBridge, University of Rochester; "Physical Properties of Microwaves": I. I. Rabi, Columbia University; "Developments in Photogrammetry During World War II": Gerald Fitzgerald, U. S. Geological Survey; "Some War-accelerated Communication Developments": O. E. Buckley, Bell Telephone Laboratories.

The American Society of Ichthyologists and Herpetologists will hold its Twenty-sixth Annual Meeting (the first since 1942) at Carnegie Museum, Pittsburgh, Pennsylvania, 16–18 April 1946. The annual banquet will be held on Wednesday, 17 April, at which time Karl P. Schmidt, chief curator of zoology, Chicago Natural History Museum, will give a presidential address on "The New Systematics, the New Anatomy, and the New Natural History."

Three members of the Society have generously provided funds for prize awards for noteworthy papers read by junior members, at both the Annual and Western Division meetings of the Society. First and second prizes of $25 and $15 in both ichthyology (including fisheries biology) and herpetology are offered, the awards to be granted only if papers of suitably high quality are presented.

The thirteenth E. Starr Judd lecture will be given by Dr. Samuel C. Harvey, William H. Carmalt professor of surgery at Yale University, on Monday evening, 15 April at 8:15 in the Medical Science Amphitheater, University of Minnesota. Dr. Harvey's subject will be: "The Healing of the Wound."

International News and Notes

Dr. Albert F. Blakeslee, visiting professor of botany at Smith College and director of the Smith College Genetics Experiment Station, has been elected an Honorary Fellow of the National Institute of Sciences of India.

Dr. E. D. Merrill, director of the Arnold Arboretum, Harvard University, was elected a foreign member of the Royal Swedish Academy of Sciences, Stockholm, to fill the vacancy caused by the death of Dr. L. Diels.

Dr. Alvin R. Lamb, Lt. Col., Sanitary Corps, has returned to his work with the Experiment Station, Hawaiian Sugar Planters Association, after five years in Army service. He served three and one-half years on the staff, Hawaiian Department and Central Pacific Area, and one and one-half years in New Guinea and the Philippines.

Dr. Oscar Riddle, now visiting professor in various South American countries under the auspices of the Department of State, has been elected to honorary membership in the Sociedad de Biologia de Montevideo and to corresponding membership in the Sociedade Brasileira de Patologia Clinica.

The State Department Report on International Control of Atomic Energy is becoming known as the Acheson Report. Dean Acheson, Undersecretary of State, was the chairman of a committee, consisting of Vannevar Bush, James B. Conant, John C. McCloy (former Assistant Secretary of War), and Maj. Gen. Leslie R. Groves, which was set up by the State Department to pass on the recommendations of the Board of Consultants who actually prepared the report. The Board consisted of: Chester I. Barnard, president, New Jersey Bell Telephone Company; David Lilienthal, chairman, Tennessee Valley Authority; J. Robert Oppenheimer, Los Alamos Atomic Laboratories; Charles Allen Thomas, vice-president, Monsanto Chemical Company; and Harry A. Winne, vice-president General Electric Company. These five men of widely different backgrounds and experience, after a study of one month's duration, concluded in complete agreement with each other that a plan for the international control of atomic energy was feasible and were also in agreement on the essentials of a plan.

Secretary of State Byrnes, in a foreword, explained that the report was not issued as a statement of policy, but as a point of departure for informed public discussion.

As President Conant had revealed earlier in an informal presentation to the Council of the AAAS at St. Louis (*Science,* 1946, **103**, 428), the plan hinges on free access to a new denatured uranium and thorium. A denaturing process, announced for the first time, would make "the material unusable by any methods we now know for effective atomic explosive unless steps are taken to remove the denaturant." It is then pointed out that any known methods for removing the denaturant would involve plants of great size and personnel of such magnitude that they could not be concealed. The report proceeds to distinguish between safe and dangerous operations. The safe activities are listed as (1) the use of radioactive material as biological tracers; (2) small nuclear reactors which can be operated at a power level low enough to be incapable of producing dangerous quantities of fissionable materials and high enough to provide neutron sources and gamma ray sources of hitherto impossible power magnitudes; (3) the development of power from the fission of denatured U–235 and plutonium, such power reactors operating in the range of 100,000 to 1,000,000 kilowatts. If no additional uranium or thorium is available to these plants, they cannot produce any further fissionable material. The operation of the plant would use up the uranium and plutonium. A minimum of supervision should make it possible to prevent the substitution of uranium and thorium for other inert materials which could be used freely.

A survey of world resources of ores yielding uranium and thorium is contemplated, and their mining is to be placed under management of a responsible United Nations agency as well as the ownership and management of the primary separation plants themselves.

The report is much too long to print in *Science,* but a printed edition of the complete text is available from the National Committee on Atomic Information, 1621 K Street, N. W., Washington 6, D. C. at $.20 a copy or $15 a hundred.

The Peking Man, taken to Japan by the Japanese army as loot during the occupation, is to be returned to the National Geographical Survey Society of China. According to Reuter, in a dispatch dated 29 December 1945, Tokyo University is reported to have surrendered the bones and artifacts to the allied authorities in Japan.

Japanese army scientists found the Peking Man in Peking after a three-year search, and specialists super-

vised its removal to Tokyo. None of the bones, utensils, and personal adornments, charts, or other documents accompanying the relics appears to have been damaged.

The formula of "Paludrine" (*Science,* 1946, **103,** 204), the new synthetic antimalarial agent, has now been announced; it is N_1-*p*-chlorophenyl-N_5-isopropylbiguanide, and is used in the form of a salt such as the hydrochloride. The drug, whose discovery was announced last November, promises to prove at least as effective as mepacrine in the treatment of malignant tertian and benign tertian malaria; and so far no toxic effects have been reported. Imperial Chemical Industries, in whose laboratories paludrine was discovered, has started limited production, and is preparing for full-scale manufacture; it is expected that it will cost less than mepacrine. Mr. F. H. S. Curd and Mr. F. L. Rose, who synthesized the drug, gave an account of its development to the Chemical Society in London on 7 February. Mr. D. G. Davey, who made biological tests of its potency, is completing a tour of Australia and India where he has been collecting the results of field trials.—*Lancet.*

The Arctic Institute of North America has reported progress in organization. In October 1945 the Institute opened its headquarters in Montreal, in quarters provided through the courtesy of McGill University. Since then the Institute has been incorporated as a non-profit-making organization in the United States under the laws of the State of New York and in Canada by Act of Parliament.

The Arctic Institute, an independent, private organization, is of international character and scope. It was financed initially by grants from the National Research Councils of Canada and the United States and by donations from private sources. During the organizational period it has seemed desirable to limit membership to the Board of Governors and the administrative staff, but the Constitution provides that a wider membership be contemplated in the near future.

At the present time the staff of the Institute consists of a small, full-time group headed by a Director with wide powers in conducting the affairs of the organization. Formulation of policy is in the hands of the Governors, chosen from among front-rank scientists and other individuals with administrative ability and interest in northern research and international scientific cooperation. The Governors serve without remuneration and meet with the Director at least three times a year to consider problems of administration and finance and to advise on the direction and coordination of research effort. They are elected triennially and serve in a personal capacity and not as representatives of the agencies, whether governmental or private, with which they are associated.

The present Board of Governors follows: Henri Bélanger, surveyor, Quebec City; Dr. Charles Camsell, commissioner of the Northwest Territories, Ottawa (past chairman); P. A. Chester, general manager, Hudson's Bay Company, Winnipeg; Dr. Henry B. Collins, Jr., director, Ethnogeographic Board, Smithsonian Institution, Washington, D. C.; Dr. Richard Foster Flint, professor of geology, Yale University, New Haven, Connecticut; Dr. L. M. Gould, president, Carleton College, Northfield, Minnesota (chairman); R. Gushue, chairman, Committee on Fishery Products, Combined Food Board, Washington, D. C., and St. John's, Newfoundland; Dr. Ernest M. Hopkins, president emeritus, Dartmouth College, Hanover, New Hampshire; Dr. Diamond Jenness, chief, Anthropological Division, National Museum of Canada, Ottawa; Dr. H. L. Keenleyside, Canadian Ambassador to Mexico, Mexico City, D. F.; Dr. C. J. Mackenzie, president, National Research Council of Canada, Ottawa; Dr. J. J. O'Neill, dean of the Faculty of Engineering, McGill University, Montreal (treasurer); G. R. Parkin, assistant treasurer, Sun Life Assurance Company of Canada, Montreal (secretary); Dr. Morten Porsild, director, Danish Arctic Research Station, Disko Island, Greenland; Walter S. Rogers, director, Institute of Current World Affairs, New York; Dr. Philip S. Smith, chief, Alaskan Division, U. S. Geological Survey, Washington, D. C.; Dr. Vilhjalmur Stefansson, 67 Morton Street, New York; Dr. A. L. Washburn, director, The Arctic Institute of North America, Montreal; and Dr. J. T. Wilson, professor of geophysics, University of Toronto, Toronto (vice-chairman).

Organization of the Caribbean Research Council

Research in the Caribbean is old and has influenced the growth and development of these islands. The work done in the past, usually directed toward resolving a pressing problem rather than toward advancing fundamental knowledge, has been sponsored by universities and government agencies—rarely, by private organizations. There are some honorable exceptions, however, in which real contributions were made to the advancement of science, but the amount of research carried out in the various communities was highly dependent not so much on the needs of the territory but on the financial conditions or the initiative and enthusiasm of its people. The result, notwithstanding, has been considerable research activity in many fields of

deavor. Much of this has been of the highest quality in the larger territories, though very little, or almost none, has taken place in the smaller and less prosperous areas. The need for coordination and for the interchange of knowledge between the workers in these various areas is obvious.

With this in mind, and pursuant to the mandate creating the Anglo-American Caribbean Commission, the Research Council was established in August 1943, as a sort of advisory board to the Commission. Its main objectives were to survey the needs of these various communities and to recommend the research to be carried out in each; to arrange for the dissemination and exchange of the results of such research; to provide for conferences between research or extension workers; and to advise what further research and cooperation should be undertaken for the benefit of the people of the Caribbean.

A provisional committee was set up in August 1943 to function for the Council until all its members should be appointed. The committee was composed of Dr. Carlos E. Chardón, director of the Institute of Tropical Agriculture of Puerto Rico, Dr. Eric Englund, chief of the Regional Investigational Branch of the Foreign Office of Agricultural Relations of the U. S. Department of Agriculture (chairman), and Mr. A. J. Wakefield, C. M. G., inspector general of agriculture of the British West Indies. The provisional committee has organized the Council and set up its various technical research committees. These committees, established within the Council to deal with special groups or branches of research, were on (1) Agriculture, Nutrition, Fisheries, and Forestry; (2) Public Health and Medicine; (3) Industrial Technology; (4) Building and Engineering Technology; (5) Social Sciences.

The Council now consists of not less than 7, and not more than 15 persons, with not less than one representative from the five research committees. Selection of members is dependent on the scientific qualifications and attainments of the individual and, as far as practicable, on the necessity of insuring a balanced representation between the several sciences and the research organizations of the area. The chairmanship of the Council is a rotating one, held in turn for one year by a representative of each of the research committees. The respective chairmen of these last-named committees were appointed by the Commission during the first year, but thereafter the committees have elected their own chairmen. The activities of these committees are coordinated by the Council.

A Central Secretariat, with a full deputy chairman as executive officer of the Council, will be established, its functions being (1) to assist the Council and its research committees in planning lines of work and in formulating proposals for the conduct and coördination of research, and (2) to promote the implementation of such work and research as might be approved by the Commission.

Before recommending the implementation of new programs, the Council considers first the necessity for compiling all of the existing scientific data and of conducting surveys that will show the conditions existing in a given area. Since agriculture is the principal occupation in most of these countries, special attention has been given to this field by the Committee on Agriculture, Nutrition, Fisheries, and Forestry. Surveys are being made on sugar, livestock, grain crops, root crops and legumes, vegetables, grasses and grassland management, and coconut, copra, and oil seeds. Of these surveys, those on sugar production and livestock are the most advanced.

A Land Tenure Symposium was held in Puerto Rico from 27 August to 3 September 1944. A general analysis of this symposium is now being prepared, which will discuss the land tenure situation in the Caribbean and which may be utilized in the future in studying and planning similarly in the agricultural programs of other geographical areas.

A Forest Research Meeting was held at Trinidad, 14–23 January 1946. The meeting had before it statements on the present state of and existing facilities for, forest research in the various territories, and on this basis drew up detailed recommendations for the future.

The Medical and Public Health Section has been especially interested in standardizing maritime quarantine throughout this area, in compiling vital statistics of these regions, in surveys in the field of nutrition, and in promoting a Congress on Public Health and Tropical Medicine, where public health problems, common to all of these countries, may be analyzed and discussed.

In spite of the many handicaps and obstacles found on the way, the Caribbean Research Council has made some good progress during its first year of life. Progress is naturally slow in an organization of this nature, but whatever steps are taken should be thorough and as definite as circumstances will permit.

As far as we know, this is the first time that an international group has joined together to study the needs, and to plan the solution, of the sundry problems vital to any geographical area. The progress of the Council bears careful watching as an example of good will and of international cooperation. There is no doubt that in the future the Council will be of ever-increasing value to the peoples it serves and, indirectly, to many other regions of the world.—*P. Morales Otero* (School of Tropical Medicine, San Juan, Puerto Rico).

In the Laboratory

A Method for Determining Bacterial Resistance and Susceptibility to Sulfonamides and Penicillin

ROGER D. REID, LT. COL., SN.C., O.R.C., and
DOROTHY TROTTER ANDERSON

Eighth Service Command Laboratory, Fort Sam Houston, Texas

Wilson (*2*) has described a method for *in vitro* testing of the resistance of Group A hemolytic streptococci to sulfonamides. Although his technic has several advantages over earlier methods, the medium he describes is extremely complicated and the average laboratory does not have the materials at hand.

The necessity for routine determination of sulfonamide resistance or susceptibility of various pathogenic bacteria caused us to attempt a modification of Wilson's medium. The results we have obtained are entirely satisfactory, yet the test is extremely simple.

Our medium has the following composition: proteose peptone #3, 10 grams; dextrose, 5 grams; sodium chloride, 4 grams; agar agar, 4 grams; and distilled water, 1,000 ml. Other peptones and modifications may possibly be used without materially affecting the results.

The reaction of the medium is adjusted to pH 7.6–7.8 before sterilization and before the addition of the drug solution. The medium is dispensed in 90-ml. quantities, and to obtain approximately 10 mg. per cent concentration of the drug in the medium, 10 ml. of 100 mg. per cent solution of the drug are added. After mixing, the medium containing the drug is dispensed in 10-ml. amounts into 16-mm. culture tubes before sterilization in the autoclave at 15 pounds pressure for 15 minutes. The final concentration of the drug can be varied by addition of the proper amount of drug and making up to 100 ml. with more basic medium.

While our experience in testing sulfonamide resistance or susceptibility has been mostly with hemolytic streptococci which grow well in the basic medium, it has been observed that other bacteria grow well also. Growth of members of the *Neisseria* is supported, although the results obtained in testing the susceptibility of the gonococci to sulfonamides with this medium have not been as satisfactory as with streptococci. From results obtained it is obvious that the medium is satisfactory for the cultivation of the majority of pathogenic bacteria. Our experience with this medium has shown that there is little or no antagonistic effect upon the sulfonamides.

Penicillin has been added to this medium in various amounts, and the susceptibility of streptococci and other bacteria to this antibiotic has been determined by this method with satisfactory results.

In the earlier tests with this medium the sulfonamides were prepared in sterile, distilled water and added to the melted medium. No contamination resulted, but addition of the drug solution to tubes required accurate measurements of both medium and drug. This is time-consuming and tedious and tends to introduce errors. It was decided to add the drug solutions to the medium before sterilization and note the effect. Parallel tests using the same medium and drug concentrations sterilized by autoclaving with the medium or added without sterilizing showed no appreciable difference on the bacteriostatic effect of the drug. The concentration of the drug in the medium was determined before and after sterilization by the method of Bratton and Marshall (*1*) for blood sulfonamide determinations. There was slight, but not appreciable, reduction of sulfonamide concentration after sterilization (Table 1).

TABLE 1

Drug	In water	Not autoclaved	Autoclaved in medium
	mg. per cent	mg. per cent	mg. per cent
Sulfanilamide	11.4	9.4	9.2
Sodium sulfathiazole ..	11.7	9.1	9.0
Sodium sulfapyridine ..	11.0	9.1	8.9

The first dilution of drug is prepared in sterile, distilled water by placing 100 mg. of the drug into 100-ml. water. The next dilution is made by adding 1.0 ml. of the first dilution to 9.0 ml. of distilled water or 9.0 ml. of the medium. It will be noted (Table 1) that there is an immediate drop in sulfonamide concentration when the drug is added to the medium. Autoclaving the drug with the medium brings about another slight drop in drug concentration. These decreases may be allowed for by the addition of slight excess of drug when added to the medium. There is no further decrease in concentration upon incubation, and the medium may be stored for two weeks, or longer, without decrease in drug concentration.

It will be seen from a glance at Table 2 that there

no difference in the results obtained with media sterilized with and without the drug.

The control (+) contained approximately 20 colonies in each case. Where growth occurred in the presence

TABLE 2

Drugs added after medium was sterilized	Concentration of drug mg. per cent	Cultures 089 MA 24	089 MA 48	N360 C71 24	N360 C71 48	147 24	147 48
Sulfanilamide	9.4	+	+	−	−	+	+
Sodium sulfathiazole	9.1	−	−	−	−	−	−
Sodium sulfapyridine	9.1	−	−	−	−	−	−
Drugs sterilized in autoclave with medium							
Sulfanilamide	9.2	+	+	−	−	+	+
Sodium sulfathiazole	9.0	−	−	−	−	−	−
Sodium sulfapyridine	8.9	−	−	−	−	−	1 colony
Control	None	+	+	+	+	+	+

of sulfonamide (Table 2) there were fewer than 20 colonies but sufficient growth to indicate resistance to 9.2 and 9.4 mg. per cent of drug. One colony appeared in medium containing 8.9 mg. per cent of sodium sulfapyridine after 48 hours' incubation.

TABLE 3

Culture	Control 24	Control 48	Sulfanilamide 24	Sulfanilamide 48	Sodium sulfathiazole 24	Sodium sulfathiazole 48	Sodium sulfapyridine 24	Sodium sulfapyridine 48
1296	+	20 colonies	0	0	0	0	0	0
156	?	10 colonies	0	0	0	0	0	0
154	+	20 colonies	0	0	0	0	0	0
153	+	34 colonies	0	0	0	0	0	0
360	+	100 colonies	0	0	0	0	0	0
1172	?	2 colonies	?	6 colonies	0	0	0	6 colonies
1467	+	>100 colonies	+	>100 colonies	+	>100 colonies	+	>100 colonies
1060	+	35 colonies		30 colonies	0	0	?	20 colonies
147	+	+	0	0	0	0	0	0
089 MA	+	+	0	0	0	0	0	0

Culture 147 is, therefore, somewhat resistant to this drug.

The convenience of preparing the medium containing the drug makes routine testing of sulfonamide resistance or susceptibility a simple matter, once the medium is prepared, amounting to no more than the inoculation of one more tube and a control tube. A series of tubes containing graduated amounts of the desired sulfonamide may be prepared. For this study a concentration of approximately 10 mg. per cent in the medium has been used and has been satisfactory in most cases for determination of drug resistance or susceptibility. Other concentrations of the drug have been used to determine degree of resistance.

Table 3 shows the results of a typical day of testing with hemolytic streptococcus cultures using 10 mg. per cent concentration of the sulfonamide indicated.

Usually results can be read after 24-hour incubation. Occasionally resistance to sulfonamide activity can be seen after 48-hour incubation and would be missed if read only in 24 hours. For this reason our results are read after 24- *and* 48-hour incubation.

Inoculation of the media for these tests is done by taking a loop of an 18- to 24-hour broth culture into a tube of tryptose-phosphate broth. One loop of this dilution into the melted (and cooled) semisolid medium containing the drug will generally give 10 to 20 colonies in the control tube. The loop that we have used measures 5.0 mm. in outside diameter and is made from 28-gauge platinum wire. The loop is flamed between each inoculation to remove traces of drug and agar and to keep the size of the inoculum as constant as possible.

While our particular interest in this problem has been to devise a simple and convenient method for testing sulfonamide resistance and susceptibility of hemolytic streptococci, the method can probably be used for testing other groups of organisms.

References

1. Bratton, A. C., and Marshall, E. K., Jr. *J. biol. Chem.*, 1939, **128**, 537.
2. Wilson, Armin T. *Proc. Soc. exp. Biol. Med.*, 1945, **58**, 130.

About the Chemical Nature of Syphilis Antigen

E. Fischer and F. Velasco

Cathedra of Anatomy and Physiology, Universidad de Chile, Santiago

In 1942 M. C. Pangborn (*3*) described a method of purifying the syphilis antigen of alcoholic beef heart extract by precipitating the phosphatides with $CdCl_2$, suspending the precipitate in petroleum ether, and eliminating the lecithin $CdCl_2$ complex by extractions with 80 per cent alcohol. The remaining solution contained cephalin $CdCl_2$ complex and antigen. After eliminating Cd by NH_3 and cephalin by precipitations with alcohol, the antigen was further purified until a substance which Pangborn claimed to be the pure syphilis antigen was obtained. According

to this author this substance, called cardiolipin, is a new, nitrogen-free, sugar-containing phospholipid, with 4.11 per cent phosphorus.

In further publications (*4, 5*) Pangborn described another method of purifying the syphilis antigen, based on the precipitation of the cephalin fraction together with the antigen by $BaCl_2$ and eliminating cephalin by alcohol. After further purification a substance was obtained with the characteristics of syphilis antigen. This second "cardiolipin" contained no sugar but approximately the same amount of phosphorus as the "cardiolipin" of the first publication.

One of the authors and his co-workers elaborated between 1931 and 1936 (cf. *1*) several methods of purifying the syphilis antigen. Having applied two of these methods successively, a purified antigen preparation was obtained recently from the phosphatid fraction of alcoholic beef heart extract. The process of purification consisted of adsorbing the antigen on specially prepared aluminum hydroxide and eluting it in benzene. The antigen was then further purified by extracting it with petroleum ether from an acidulated 80 per cent alcohol solution. From 207 grams phosphatides 1 gram of a purified antigenic preparation was obtained, with only 0.01 per cent phosphorus, 0.25 per cent reducing substances (liberated by acid hydrolysis), and 40 per cent fatty acids (liberated by alkaline hydrolysis) (*1*).

It was shown in 1936 (*2*) that by extracting an 80 per cent alcoholic solution with petroleum ether, only a part of the antigen could be obtained in the petrol ether solution, another part still remaining in the hydroalcoholic phasis. Only after acidulating this phasis with HCl did the antigen disappear completely from it, entering into the petroleum ether phasis. We may assume, therefore, that the antigen occurs in two different forms in the alcoholic organ extract, *i.e.* acid and salt.

In recent experiments we have worked on the phosphatid fraction of 10 beef hearts, obtained by extraction with alcohol and precipitation with acetone. The antigen was absorbed on aluminum hydroxide and eluted in benzene. The substance obtained in this way was dissolved in 80 per cent alcohol and extracted at first without, and then with, acidulation.

We obtained in this way two fractions, which we shall call "petroleum ether fraction before acidulation" (P.E.N.) and "petroleum ether fraction after acidulation" (P.E.A.). Both fractions reacted with strongly positive sera. P.E.N. weighed 39 mg., and no phosphorus could be detected in it. P.E.A. amounted to 22 mg. with 0.1 per cent phosphorus. Both fractions were yellow oils which hardened rapidly, forming a transparent, soft film.

We assume that the small quantities of phosphorus found in our preparations correspond to impurities as was the case with the reducing substances in our former experiment.

References

1. FISCHER, E., FISCHER-DALLMANN, R., and BONÉ, R. *Immunol.*, in press.
2. FISCHER, E., STEINERT, J., and FISCHER-DALLMANN, R. *Z. Immunitäts.*, 1936, **89**, 133.
3. PANGBORN, M. C. *J. biol. Chem.*, 1942, **143**, 247.
4. PANGBORN, M. C. *J. biol. Chem.*, 1944, **153**, 343.
5. PANGBORN, M. C. *J. biol. Chem.*, 1945, **157**, 691.

A Cheap and Speedy Method of Cleaning Old Microscope Slides

G. J. SPENCER

Department of Zoology, University of British Columbia, Vancouver

For years our Department has been faced with the problem of cleaning off old microscope slides made with Canada balsam. None of the solvents used (xylene, toluene, turpentine, and coal oil) has proved effective in less than two weeks, and the resulting mass of dilute balsam, slides, cover slips and slide labels provided another problem in cleaning up.

Recently while collecting ectoparasites of mammals by the method recommended to me by Dr. G. H. E. Hopkins, of Uganda, which originated from Dr. F. L. Werneck, of Brazil, it occurred to me to try this upon microscope slides; it worked like a charm and is proving a boon in our laboratories.

Dr. Hopkins' method of recovering ectoparasites from fur is to place portions of hide into hot, 10-per cent caustic soda; the soda dissolves the hair and fur, and the sludge is then washed through fine, stainless steel mesh which retains the parasites. I have used this procedure extensively for parasite recovery, with considerable success, and now it is proving invaluable for cleaning slides. A number of methods can be employed, but I use three 500-cc. beakers, two of 10-per cent caustic soda on tripods over low Bunsen flames, and one spare. The caustic is kept at nearly boiling point, and a row of slides, held in a spiral of copper wire with the two ends sticking out straight, is placed across the top of the beaker so that the glass is immersed for most of its length. A large number of slides, from 1 to 13 years old have been tested and the speed of action timed; the latter varies inversely as the age and the amount of balsam present. In the case of old slides with thick balsam, the labels and cover slips slide off in from 23 to 30 seconds; in year-old slides with little balsam, it may take up to two minutes for the cover slips to fall off. All slides made with very little balsam, irrespective of age, take longer than those with much balsam. The size of cover slip does not affect the speed of action.

50-mm. rectangles come off as fast or even faster than 18-mm. circles unless the long ones are overlapped by a label which is not entirely immersed in the caustic.

The slides must not be in contact or else the hot caustic cannot penetrate between them. If any cover slip does not drop off in two minutes, it can readily be shoved off with the edge of a slide.

When all cover slips and labels have fallen off, the beaker is left over the flame for about a minute or two longer, the slides are released from the spiral, the caustic soda is poured off into the spare beaker, and another set of slides in a holder is set to soak. In the meantime the beaker with slides and cover slips is held under a gentle flow of hot water in the sink. The hot caustic soda apparently saponifies the esters in the Canada balsam, and the hot water washes it all away, leaving both slides and cover slips beautifully clean. If any balsam remains adhering to the glass, it can usually be washed off between thumb and finger under the tap; occasionally an obstinate one must be dropped back into the hot caustic to soak.

By the time one has carefully washed 10 slides and their cover slips between thumb and finger under the tap and dried and boxed them, the next series of 10 is ready for washing. It is therefore unnecessary to have a larger setup.

A more convenient method than the one outlined above, would be to have a wire-gauze box of copper or stainless steel with a spiral or slotted holder on top, so that the whole thing could be suspended in a large beaker of caustic and the box and its contents lifted out instead of having to pour the alkali from one beaker to another. In the method just described, additional caustic solution has to be added from time to time to the beaker over the flame to make up for the amount washed away under the tap. This periodic addition of new solution seems to keep up the effectiveness of the hot bath, which does not become saturated and therefore impotent until many slides have been cleaned.

Solutions of 10, 15 and 20 per cent have been tried. The 10-per cent solution seems to work as well as the stronger ones. Leaving slides to soak overnight, or even for days, in cold caustic is quite ineffective and seems to render the balsam somewhat resistant to saponification when the slides are finally placed in a hot solution.

Letters to the Editor

Sources of Our Future Scientists

Vannevar Bush, Director of OSRD, has estimated in his recent report to the President (*Science, the endless frontier*) that the deficit of those who would have received a bachelor's degree in science or technology had reached 150,000, and that by 1955 there would be a loss of 17,000 who would otherwise have been given advanced degrees.

There is, however, one important element in the supply of future scientists which he did not consider. This is the source of the hereditary material, the necessary biological counterpart of the favorable educational environment which he discusses. All recent studies of this indispensable prerequisite for future scientists are alarming, indicating as they do that for the past century our most educated groups have failed to bear enough children to replace themselves. These studies have, of necessity, been based upon the ability to acquire a given amount of education, usually that represented by a college degree. For economic reasons, this test does not include all who might have become graduates, but it does indicate an intelligence level well above that of the average in the country. While there will obviously be exceptions, it seems fair to assume that the average scientific ability of the offspring will also be high, and that the surroundings and mental stimulation to which these children will be exposed will be favorable for the production of scientists.

While graduates of Yale in the early 1700's had averaged about 5 surviving children each, this record steadily decreased. For the classes graduating about 1825, 3.5 children were born to each graduate; for those graduating in the decade from 1870 to 1880 from Harvard, Wesleyan, Syracuse, and Yale, the children were well below the number necessary for replacement. For the Harvard classes of the 1890's, they had fallen to 1.45 per graduate. To secure later information, the writer has made a study of the five most recent Harvard classes to have issued their 25-year reports (The deficit in the birthrate of college graduates. *Hum. Fertility,* in press). These give statistics collected at a time when their families are nearly complete. A more favorable trend was found, with 1.67 children per graduate, but the offspring are still distinctly below the replacement level. Furthermore, it may be only a transient increase, since reports of the classes of 1931 and 1936 disclose that in the early years after graduation, their children were only 77 and 62 per cent of the per-capita rates of 1916 to 1920 for the same periods.

Ominous figures are also found in the recently published volume of the U. S. Census Bureau (*Population, differential fertility 1940 and 1910, women by number of children ever born.* 1945). Women included in the 1940 census, aged 45 to 49 and with less than 4 years of schooling, reported an average of more than 4 children each. As the amount of education increased, this number fell until for high school and college graduates it was 1.75 and 1.23, only 77 and 55 per cent of the number of children necessary for the replacement of the parents. The Census Bureau estimates that for one son per father (or daughter per mother) to survive to the age at which his father (or her mother) was enumerated, 2.22 children must be born. With the better than average care given by college graduates, the number is somewhat less than this for that group.

To determine the extent of this loss of an important national resource, a study of the numbers of children born to the graduates of other colleges seems of value. The Population Reference Bureau, 1507 M St., N.W., Washington 5, D. C., has, therefore, planned a nation-wide intercollegiate comparison of these birth rates. Questionnaires have been offered without charge to those wishing to assemble the needed information from the classes of 1921 and 1936, the twenty-fifth and tenth reunion classes. The earlier class was chosen because few children are to be expected after this date; the later class, to indicate the more recent trend.

Sixty-six colleges, with about 26,000 students in these two classes, have asked for the questionnaires. The results should give valuable information regarding the sources from which our future scientists may be expected, and the degree to which our present educated groups are replacing or failing to replace themselves.

CLARENCE J. GAMBLE, M.D.
255 Adams Street, Milton, Massachusetts

B-Glycoside Formation in Plants From Absorbed Chemicals

The letter by E. G. Beinhart (*Science,* 1946, **103**, 207–208) with reference to the absorption of the vapors of phenols by plants is of interest in calling attention to the relative ease with which absorption and retention of non-naturally-occurring organic compounds may take place. Experiments conducted several years ago by the writer (see, for example, *Science,* 1940, **92**, 42–43, and *Contr. Boyce Thompson Inst.,* 1943, **13**, 185–200) showed that various chemicals containing an alcoholic or phenolin hydroxyl group were readily absorbed from nutrient solutions (and in several cases, inadvertently from vapor in the air) and combined within the plant with sugars to form β-glycosides. Such a biosynthesis of glycosides seems to take place quite generally among higher plants, and it appears likely that the phenols with which Beinhart's article is concerned were fixed within the plants as β-glycosides. This would explain the persistence of the flavor and the lack of off-flavors in the root crops (carrots, beets, and potatoes), since these glycosides do not seem to move readily from one organ of the plant to another.

In view of the stability of these β-glycosides with the plant it follows that the presence of relatively sm amounts of chemical in the air over a long period time could result in the building up of appreciable co centrations of foreign β-glycosides in the edible portio of plants. The hazard is thus much greater with chem cals that undergo this or similar reactions than wi those that are not fixed by the growing plants.

LAWRENCE P. MILL
Boyce Thompson Institute for Plant Research, Inc.
Yonkers 3, New York

On Recognition of High School Science Training

Charles A. Gramet's letter on High School Scienc (*Science,* 1946, **103**, 149) brings up a point on which can report two observations, one personal and one pro fessional, but both illustrative of the serious influenc which the college attitude toward high school scienc has on a student's planning of his academic work an his preparation for gainful employment.

In 1916, when I was 12 years old, my father followe the rather unusual expedient of arranging for me t spend a summer term studying chemistry in compan with a friend of the same age. At the conclusion o this term our instructor informed our parents and th school authorities that we had quite satisfactorily com pleted the equivalent of a rather stiff first term o senior high school, or first year college, chemistry.

Later, because I was interested and did not mind the duplication of the first term of work, I took a fu year of chemistry in my senior year at East High School, Rochester. With no further training in chem istry I carried out some work in my father's anatomical laboratory which required careful chemical manipula tion; I held a job for nine months as an assistant to a photochemist in the Eastman Kodak Research labora tory; and I later did considerable writing on subject which required some basic knowledge of chemistry.

Obviously, I was interested in chemistry. I consid ered certain college courses permitting advanced work in chemistry, but in two instances I met with an absolute refusal by colleges to accept this excellent preparatory training as an equivalent of first year college chemistry. A similar experience took place in relation to biology. After a boyhood and youth spent in close contact with the various Ward family activities in anatomy and the biological sciences, and a year of an excellent senior high school biology course, my college would not give credit for senior high school biology and I took first year college biology. It differed little from the high school course and, in essence, was so much waste motion.

I have just gone back to some of my letters, written in first year college in 1922, and I find that the need to "repeat chemistry and biology" was a constant consideration which led me to make some rather drastic changes in my college plans and to swing over to journalism and sociology. This was not a student whim; it was a carefully considered reaction to the waste of time and boredom of repeating high school science courses.

In the period since 1934, when I have been working a vocational counselor for out-of-school youth and lts and have been teaching other counselors engaged this work, I have time and time again encountered ng men and women who have been quite needlessly ced to undergo the drudgery of repeating their high ool chemistry and/or biology in the first year of llege, or have been influenced to make very drastic nges in their education-vocational plans by this regution.

I do not think that I need to stress, in this enlightd age, that the motivation of interest is probably e most potent force we can arouse in the classroom. also think that many thoughtful educators will not htly dismiss youthful disinclination to repeat science urses—it smacks of the Middle Ages to talk of "discipline" as an excuse for enforcing monotonous repetition.

It might also be suggested that in many senior high chools the size of classes and the quality of teaching superior to the overcrowded classrooms and laboratories and the routine type of instruction found in many first year college science courses.

It is granted that some standards are needed. High chool science instruction, in chemistry, physics, and iology, varies a great deal in various states. However, if the college science faculties and committees on admissions can bring themselves to evaluate the quality of cience teaching in various states and even in various municipalities within states, they can eliminate a practice which experienced vocational counselors can testify is either driving students to abandon plans for scientific work or exposing them to an educational ordeal which is inclined to cause youthful doubt as to whether education really lives up to the enlightened claims in which it is so prone to indulge.

I am not prepared to agree that college admissions authorities should "require" a two- or three-year high school science sequence as a prerequisite to college admission. College admission requirements are inflexible enough as it is, but it is reasonable to suggest that college science faculties give the same recognition to high school science work, in well-conducted courses in chemistry, physics, and biology, as is given by language and mathematics faculties to high school work in those fields.

This encouragement of high-quality work in chemistry, physics, and biology in high school, rather than the science survey courses, will also assure that high school students who do not go to college will have some adequate knowledge of scientific progress and problems, useful either in their future orientation in business or in the skilled trades.

ROSWELL WARD
School of Education, New York University

Recent Additions to the Dudley Herbarium

By the terms of the will of the late Dr. L. Herman Knoche, of San Jose, California, Stanford University has received his entire herbarium and botanical library. The herbarium specimens and the famous collection of botanical reprints assembled by Adolph Engler have been moved into the quarters of the Dudley Herbarium and are already available for use by qualified graduate students enrolled at Stanford, by the staff, and by other investigators interested in taxonomy, ecology, and geographical distribution of plants.

The bulk of Dr. Knoche's herbarium (totaling over 125,000 sheets of dried specimens) was accumulated by Gaston Gautier and consists, for the most part, of specimens collected in southern Europe and other areas adjacent to the Mediterranean Sea. This collection contains a large number of specimens cited by various European authors and is very valuable to botanists of the Western Hemisphere who wish to study authentic material from southern Europe and northern Africa. A few scattered specimens from other parts of the world are also included, but these are decidedly in the minority. None of these specimens is mounted, all of them being laid between sheets of thin paper, the labels being tucked under the stems or leaves of specimens to which they apply. In most cases only one collection is represented on a sheet, but in a few cases two separate accessions have been placed in the same double sheet. Those that have thus far been examined are quite distinct in appearance when two are on the same sheet, so no serious difficulty is anticipated in separating them and getting them segregated onto individual herbarium sheets. The bundles are arranged systematically, and any desired family or genus can be extracted readily for study.

Engler's collection of reprints covers several broad fields in botany in addition to strictly taxonomic treatments of vascular plants. Sections of it deal with geographical distribution, ecology, plant physiology, morphology, floristic studies of various regions, and small sections on algae, fungi, mosses, liverworts, and ferns. The taxonomic parts were arranged according to families, following the Engler and Prantl system, and have been kept in the same order in which they were classified by Engler himself. Many of the folders in which loose reprints are tied still bear the labels written in Engler's hand. The collection contains over 25,000 separates.

The library of bound botanical books is rich in floras from many parts of the world and contains a number of comparatively rare works not generally available in the libraries of the western United States. This portion of Dr. Knoche's library has not yet been catalogued and placed at the command of the botanists working on the Stanford campus, but it is hoped that this task will go forward steadily and that the entire library will be available for use within a few months.

IRA L. WIGGINS
Stanford University

New Use for DDT

"Scab mites" (*Psoroptes cuniculi*) often cause extensive scab formation in the ears of laboratory rabbits. These mites do not burrow beneath the skin, but remain

on the surface, where they may cause sufficient irritation to produce a many-layered scab in which they may be present in large numbers.

We have found that the application of a 5-per cent solution of DDT by an ordinary nebulizer to the inner surface of the ear of the rabbit affords a simple, nontoxic method of curing this condition. When the scabs are many layered, it may be necessary to make several applications of DDT at three-day intervals in order to reach the more deeply situated parasites. The destruction of the parasites is followed rapidly by the healing of the affected surface. A single application is useful in the prophylaxis of exposed animals.

ERNST T. KREBS, JR.
Division of Anatomy
University of California Medical School, San Francisco

Book Reviews

Photosynthesis and related processes. **Vol. I: *Chemistry of photosynthesis, chemosynthesis and related processes in vitro and in vivo.* Eugene I. Rabinowitch. New York: Interscience Publishers, 1945. Pp. xiv + 599. (Illustrated.) $8.50.**

In the last 25 years our knowledge about photosynthesis has undergone a luxuriant growth. At the beginning of this period Stiles and Spoehr each summed up the available data in monographic form. Since then information has merely accumulated; and while there have been efforts to weed and cultivate small sections, the field as a whole has not had the intensive examination and harvesting it has needed and deserved.

The task is formidable; its extent is indicated by the fact that the present book is only the first of a pair planned to cover the subject. This volume deals with the chemical phases of photosynthesis, while its promised successor is to treat the physical aspects.

The book contains 20 chapters. The first two are introductory and place the subject in its scientific and historical setting. The next eleven chapters take up the photosynthesis reaction as a whole, its products, related reactions outside the cell, chemosynthesis by bacteria, the photochemical reactions, the nonphotochemical reactions, and the effects of outside chemical agents. The seven chapters that follow describe the pigments involved in photosynthesis, their structure, chemistry, and photochemistry. A final chapter covers the relations between photosynthesis and respiration.

There is a large number of original diagrams, tables, and figures. Also, there are excellent author and subject indexes. Each chapter ends with a bibliography arranged historically. A rough count adds up to about 2,000 titles.

The treatment of this extensive material is fresh and tough-minded. Every contribution to photosynthesis and the related subjects has been read and evaluated, and is given a presentation which is just and rigorous.

The book, however, is no pedestrian account of work accomplished. The first chapter is beautifully written; it has a magnificence of conception that carries one along breathlessly. Similarly, Chapter II, which describes the discovery of the basic phenomena of photosynthesis, maintains a fine balance between large issues and detailed data and gives one a sense of participating in the high adventure of scientific discovery. Even Chapter III, which has no historical structure, is fascinating reading because of the sheer intellectual power of its analytical procedure.

Naturally, such an exciting level of writing cannot be maintained, and the price which has to be paid for the patient, inclusive, and critical presentation of so large a collection of material is an absence of the dramatic power of an historical narrative. Since one does not ordinarily find this in a scientific monograph, we may gratefully accept these first three chapters as the *hors d'oeuvre* of a nourishing meal furnished by the rest of the book. The chapters which follow are not just to be read; they need to be studied. And for this too we are grateful. We need the careful and detailed discussion of all this wealth of data for the edification of scholars in this field and for the instruction of those just entering it. Dr. Rabinowitch is to be congratulated on the high level which he has maintained in working over this staggering mass of information.

With so much excellence already received, it may seem ungracious to ask for something else. Yet one wishes that Rabinowitch had not divided the subject into the obvious chemical and physical volumes. Photosynthesis is all of a piece; its division into physics and chemistry is artificial and produces difficulties which are apparent even to the author. Perhaps the situation will be improved when the physical companion volume appears, so that one can easily refer from one volume to the other.

Also, one misses a chapter or two in which the larger outlines of the subject are delineated. The same boldness, which in Chapter II omitted details in order to bring out the essential features of photosynthesis as recognized in the early days, could have been used to paint a broadly conceived picture of the essentials of today. One would like to see in sharp relief such concepts as the light and dark reactions, quantum efficiency, limiting factors, the effect of light intensity and of intermittent illumination, so that the reader might have clearly before him the large masses of the composition before he stops to examine the details which enrich and enliven the separate parts.

Nevertheless, even the elaborate and detailed presen-

tation has its virtues. For example, we cannot but become impressed with the relation of photosynthesis to other biological activities which build organic compounds by reducing carbon dioxide. Some plants require light but use H_2S as a reductant instead of H_2O. Others do not even require radiation, but rely on the energy they get from simple organic substances. The pattern is the same, but the specific means vary. This hierarchy of CO_2 reduction processes may help us imagine the origin and development of photosynthesis. It shows us simpler systems which could have furnished energy for life before the invention of chlorophyll, a substance which is high in the structural scale and needs living tissue for its manufacture.

This is a great book, which will serve for many years as *the* source book of critically digested information about photosynthesis. It is to be hoped that Rabinowitch will not keep us waiting too long for the second volume and that, having acquired all this erudition about photosynthesis, he will take his learning lightly and write a small book for the uninitiated so that the general scientific public may profit from his prodigious labors.

SELIG HECHT

Columbia University

Sampling statistics and applications: fundamentals of the theory of statistics. **James G. Smith and Acheson J. Duncan. New York and London: McGraw-Hill, 1945. Pp. xii + 498. (Illustrated.) $4.00.**

This volume is a very well-presented combination of advanced statistical method and both elementary and advanced sampling theory. It is intended for advanced students and research workers and is gauged at a level which makes a thorough knowledge of elementary statistics a prerequisite to its enjoyment and comprehension. However, granted a thorough training in the elements of statistics, basic concepts and definitions in advanced theory are clearly presented. Symbols are well defined, and the scope of mathematical treatment is chosen in a manner which makes the volume very valuable as a text and as a reference book.

After the general theory of frequency curves has been discussed, the theory of random sampling is presented in Part II, proceeding to an advanced exposition in Part III. Parts II and III deal with important sampling considerations not usually found in statistical texts. The advantages and necessities of random sampling are discussed, and a very careful treatment of the practical difficulties encountered in the use of random sampling is included. In this connection the authors explain why it must be admitted "that confidence in an inference based on a random sample is dependent on the 'thought' or firm belief that it is a truly random sample. Whether thought with respect to randomness is any sounder, as a basis for inferences, than thought with respect to representativeness of a sample obtained by some other method is a debatable question." Recent conflict of theory among experts indicates the vital significance of this consideration.

A portion of the section devoted to elementary s
pling theory discusses the value of stratified or re
sentative random sampling. The authors point out
value of stratification when it is based on correlates w
the survey objective. They recognize a reduction
error when proper representation is achieved: "The s
nificance of stratified or representative random samp
is that it reduces sampling errors."

Sampling is discussed in relation to the assembly
evidence and also in relation to the estimation of po
lation parameters. This allows an extension of t
theory to our ordinary statistical conceptions of rel
bility and confidence. The boundaries of statistical i
ference are defined, and examples of their application a
given.

RAYMOND FRANZ

10 Rockefeller Plaza, New York City

The bacterial cell. **René J. Dubos (with an addendum b
C. F. Robinow). Cambridge, Mass.: Harvard Uni
Press, 1945. Pp. xix + 460. (Illustrated.) $5.00.**

This thought-provoking discussion integrates o
knowledge of the biological and chemical architecture o
bacteria with the classical techniques of cytology an
interprets some of the phenomena of the infectio
process in terms of the biochemical architecture of th
bacterial cell. The author makes the point in his Prefac
that "in addition to physicochemical properties share
by all living forms, each bacterial type possesses a struc
tural and biochemical individuality which could serve as
a basis for an orderly statement of the problems of
cellular organization, and for a rational system of
classification based on phylogeny." Known facts, how
ever, are too few for convincing integration and gen
eralization—thus a plea for more fundamental investi
gations in the field of bacterial physiology.

The volume is the outgrowth of a course of eight
lectures delivered under the auspices of the Lowell In
stitute in Boston. The chapter titles are important
enough to note: "Materials, Problems and Methods,"
"Cytology of Bacteria," "Physicochemical and Stain
ing Properties of Bacteria," "Analysis of Cellular
Structure by Biochemical and Biological Methods,"
"The Variability of Bacteria," "The Nature of Viru
lence," "Immunization Against Bacterial Infection,"
"Bacteriostatic and Bactericidal Agents," and "Trends
and Perspectives." The addendum is entitled "Nuclear
Apparatus and Cell Structure of Rod-shaped Bacteria."

The author discusses the many controversial questions
impartially and with credit to the protagonists of both
sides. Where final conclusions are unwise, they are not
made by the author.

The author's statement, "Even among the Eubac
teriales—the so-called true bacteria—one finds strange
bedfellows, such as small Gram-negative autotrophic
organisms, the Gram-positive proteolytic spore formers,
acid-fast bacilli, which differ so profoundly from each
other in metabolism, structure and even mode of divi
sion as to have little in common except microscopic

ensions," should engender lively discussion. Per- "the methods employed by bacteriologists rather the biological material" are defined by the micro- ic size of the bacteria which impose certain physical chemical characteristics, rather than the biological erial.

In speaking of the phylogeny of bacteria, if we ept with the author the principle of "retrograde lution by loss of certain characters," one may beg question in reasoning that heterotrophs preceded otrophs. The latter possess so many physiological lities, e.g. formation of vitamins and enzymes, that argument works both ways, and no conclusion is ched. Apparently we have not determined what are essential losses which constitute "retrograde evolu- n" or "loss variation."

Until the Twentieth Century bacteriology was a ience of new forms of life without much regard to ivities. The great productivity era in bacteriology me with the realization that bacteriological phenomena nstitute events of great importance to man—transfor- tion of organic matter and parasitism. During the st few decades the problems of bacteriology have been ated in terms of the classical sciences and of the evalent biological, physiological, and biochemical phi- osophies. Dubos points out that much of our theoreti- l knowledge was a by-product of the solution of prac- ical problems by empirical methods, and examples are iven of the practical advantage of theoretical knowledge, g. development of vaccines, therapeutic sera.

Bacterial specificity is discussed from the point of iew of its various levels, *i.e.* strain, species, genus, etc., nd of its type, *i.e.* immunologic, enzymic, structural, or biochemical.

The author points out that a too narrow interpretation of the dogma of the fixity of bacterial species led to a neglect for nearly 50 years of one of the most intriguing and important characteristic properties of the bacterial cell, namely, its ability to undergo environmental and hereditary transformations. Final recognition of this phenomenon suggested powerful and original techniques for the study of cellular organization and provided new points of view which define the place of bacteriology among the biological sciences.

Pertinent to the systematic chaos occurring in the classification of bacteria is the statement to the effect that in the description of bacterial groups (e.g. species) descriptive characters are used which are precisely those that have been found to undergo variation. It seems likely that the progress of bacterial taxonomy and the study of evolutionary trends among bacteria will require that cultures be described in terms of their multiple potentialities and not of an accidental phenotype.

The chapters are well organized and interestingly written. The reviewer appreciated particularly the author's discussions of bacterial variability (Chap. V) and bacteriostatic agents (Chap. VIII). This book is essential to bacteriologists, biochemists, and biologists.

C. H. WERKMAN

Iowa State College, Ames, Iowa

Scientific Book Register

ÅBERG, EWERT. *Studies of crop production in the United States 1940 to 1943.* Uppsala, Sweden: Almqvist and Wiksells Boktryckeri AB, 1944. Pp. 86. (Illustrated.)

BEET, ERNEST AGAR. *A text book of elementary astronomy.* Cambridge: at the Univ. Press, 1945. Pp. x + 110. (Illustrated.) $2.00.

BOURGOUIN, LOUIS. *Histoire des sciences et de leurs applications.* Montreal: Editions de L'Arbre. Pp. 326. (Illustrated.)

BRUES, CHARLES T. *Insect dietary: an account of the food habits of insects.* Cambridge, Mass.: Harvard Univ. Press, 1946. Pp. xxvi + 466. (Illustrated.) $5.00.

BRUNSCHWIG, ALEXANDER, *et al. Cancer; what the public should know; a radio discussion.* (Transcript No. 403.) Chicago: Univ. Chicago Round Table, 1945. Pp. 17. $.10.

BURTON, E. F., and KOHL, W. H. *The electron microscope: an introduction to its fundamental principles and applications.* (2nd ed.) New York: Reinhold, 1946. Pp. 325. (Illustrated.) $4.00.

BUSH, VANNEVAR. *Endless horizons.* Washington, D. C.: Public Affairs Press, 1946. Pp. ix + 182. $2.50.

CLARK, BRUCE L., and DURHAM, J. WYATT. *Eocene faunas from the department of Bolivar Colombia.* (Geol. Soc. Amer., Mem. 16.) Baltimore: Waverly Press, 1946. Pp. vi + 126. (Illustrated.)

COHN, ALFRED E. *Minerva's progress: tradition and dissent in American culture.* New York: Harcourt, Brace, 1946. Pp. viii + 101. $2.00.

COLE, FAY-COOPER. *The peoples of Malaysia.* (2nd printing.) New York: D. Van Nostrand, 1945. Pp. xiv + 354. (Illustrated.) $4.00.

COOLIDGE, JULIAN LOWELL. *A history of the conic sections and quadric surfaces.* Oxford, Engl.: Clarendon Press, 1945. Pp. xi + 214. $6.00.

DUNLAP, ORRIN ELMER, JR. *Radar; what radar is and how it works.* New York: Harper, 1946. Pp. 222. (Illustrated.) $2.50.

FOWLER, WILLIS M. *Hematology for students and practitioners.* New York-London: Paul B. Hoeber, 1945. Pp. viii + 499. (Illustrated.) $8.00.

GAUTHERET, R. J. *La culture des tissus: une voie nouvelle en biologie végétale.* (L'Avenir de la Science—21.) France: Librairie Gallimard, 1945. Pp. 203. (Illustrated.) 190 fr.

GOLDZIEHER, MAX A. *The endocrine glands.* New York: Rudolf Schick, 1945. Pp. 49. (Illustrated.) Textbook, $1.20; charts, $6.50 each.

GRANT, JULIUS. (Ed.) *Hackh's chemical dictiona American and British usage.* (3rd ed.) Philadelp Toronto: Blakiston, 1946. Pp. xii + 925. (Illustrate $8.50.

HAYES, JOHN E. R. *The nature of patentable in tion: its attributes and definition.* Cambridge, Ma Addison-Wesley Press, 1945. Pp. vi + 183. $5.00.

HERRICK, ARTHUR D. *New drugs.* New York: Rev Publishing Co., 1946. Pp. xiv + 303. $4.00.

HIRSCH, A. A. *Manual for water plant operato* Brooklyn, N. Y.: Chemical Publishing Co., 1945. P 403. (Illustrated.) $6.50.

KENNEDY, RAYMOND. *Bibliography of Indonesian p ples and cultures.* (Yale Anthrop. Stud., Vol. 4 New Haven, Conn.: Yale Univ. Press, 1945. Pp. 2 (Illustrated.) $2.50.

MURRILL, WILLIAM ALPHONSO. *Reptiles good and b* Gainesville, Fla.: Univ. Florida, 1945. Pp. 32. (Illu trated.) $2.00.

MURRILL, WILLIAM ALPHONSO. *Rocks.* Gainesville, Fla. W. A. Murrill, 1946. Pp. 62.

RAPAPORT, DAVID. *Diagnostic psychological testing* (Vol. 1.) Chicago: Year Book Publishers, 1945. Pp 573. (Illustrated.) $6.50.

RIDER, JOHN F. *Inside the vacuum tube.* New York John F. Rider, 1945. Pp. xvi + 407. (Illustrated. $4.50.

SMILLIE, WILSON G. *Preventive medicine and public health.* New York: Macmillan, 1946. Pp. xvi + 607 (Illustrated.) $6.00.

SMITH, BRUCE LANNES, LASSWELL, HAROLD D., and CASEY, RALPH D. *Propaganda, communication, and public opinion: a comprehensive reference guide.* Princeton: Princeton Univ. Press, 1946. Pp. ix + 435 $5.00.

SPURR, J. E. *Geology applied to selenology.* I: The Imbrian Plain region of the moon (2nd printing); II: The features of the moon. Lancaster, Pa.: Science Press, 1945. I—Pp. x + 112; II—Pp. xiii + 318. (Illustrated.) $5.00.

STEACIE, E. W. R. *Atomic and free radical reactions: the kinetics of gas-phase reactions involving atoms and organic radicals.* (Amer. Chem. Soc. Monogr. Ser.) New York: Reinhold, 1946. Pp. vii + 548. $8.00.

THEILHEIMER, W. *Synthetische Methoden der organischen Chemie.* (Repertorium, Vol. I.) New York-Basel: S. Karger, 1946. Pp. viii + 224. Fr.s. 25.

WELLS, A. F. *Structural inorganic chemistry.* Oxford: Clarendon Press, 1945. Pp. viii + 590. (Illustrated.) $7.50.

ZOBELL, CLAUDE E. *Marine microbiology: a monograph on hydrobacteriology.* Waltham, Mass.: Chronica Botanica, 1946. Pp. xv + 240. $5.00.